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LONDON SATURDAY JANUARY 2 1954

CORTISONE AND A.C.T.H. IN TREATMENT OF NON-RHEUMATIC CONDITIONS

BY

G. M. ABER, M.B., Ch.B.
Registrar

AND

G. N. CHANDLER, B.M., M.R.C.P.
Senior Registrar

S. J. HARTFALL, M.D., B.Sc., F.R.C.P.
Professor of Clinical Medicine

(From the Department of Clinical Medicine, University of Leeds, and the General Infirmary at Leeds)

Since cortisone and A.C.T.H. were made available in this country in 1951, 78 patients have been treated with these drugs at the General Infirmary at Leeds. In no case has the decision to start the treatment rested on conditions other than therapeutic indication, so that our experience, though fairly broadly based, has been gained more from individual needs than from research interest.

In non-rheumatic conditions the results obtained seem valuable enough to allow of an interim report on our conclusions. Patients in this group have been submitted to treatment not only where it was felt that cortisone or A.C.T.H. offered the best hope of improvement, but also in an attempt to elucidate their various and varying effects in disease processes. Due weight has been afforded these aims in the allocation of cortisone or A.C.T.H. for individual patient treatment, applications for the drugs being submitted to the cortisone committee at the infirmary, one of us (S. J. H.) acting as secretary to this panel.

This report summarizes the results and experience gained in the non-rheumatic diseases. Fourteen patients have been observed with disorders of the blood and blood-forming organs; 16 patients have been treated for disease or dysfunction of the endocrine glands; and in a third, miscellaneous, group the effect of treatment has been studied in two patients with cirrhosis and portal hypertension, in two patients presenting a nephrotic syndrome, and in nine patients suffering from asthma.

No attempt has been made to review the literature, since this is thought to fall outside the scope and intention of a report which deals, in the main, with the routine treatment of problems common to a general teaching hospital.

DISEASES OF THE BLOOD

Acute Acquired Haemolytic Anaemia

Four children, whose ages ranged from 6 months to 8 years, were admitted to hospital during a period of 16 days in March, 1952, suffering from acute acquired haemolytic anaemia. Because of the poor response of three of them to blood transfusions a trial was given to the use of A.C.T.H., and the results have been reported elsewhere in greater detail (Rose and Nabarro, 1953).

Clinical Presentation.—All described a short febrile illness characterized by lethargy, irritability, increasing pallor, breathlessness, and haemoglobinuria; two showed moderate icterus, one of these also demonstrating enlargement of the spleen, liver, and lymph nodes. They were acutely ill, and in no case were any specific aetiological factors evident.

Haematology.—The findings in the peripheral blood were of a severe haemolytic process without evidence of leukaemia. The sternal marrow in the two patients on whom this examination was performed showed only normoblastic hyperplasia. The direct Race–Coombs test was positive on admission in two patients and eventually positive in three.

Treatment.—Three of the children required the protection of A.C.T.H. or cortisone. The fourth responded to a single blood transfusion given on the seventh day after admission, and she remained in good health despite persisting hepato-splenomegaly. Of the three treated with hormones, a girl aged 3 who had relapsed rapidly after each of three transfusions responded to a course of A.C.T.H. given over a period of five weeks, begun at an initial dosage of 50 mg. daily intramuscularly and gradually reduced after three weeks. A second child, a boy aged 8, was given A.C.T.H. because of severe relapse after several transfusions. He responded well to a dosage of 100 mg. daily continued for two weeks, gradually reduced in a "steppage" procedure in the next three weeks, but he relapsed when A.C.T.H. was discontinued. After further transfusion, splenectomy was performed without apparent effect. A second course of A.C.T.H. (100–75 mg. daily) was given, to which he again responded. In the seventeenth week after admission cortisone was substituted for A.C.T.H. A final attempt at drug withdrawal resulted in brisk haemolysis and he still required 75 mg. of cortisone daily, nearly 60 weeks after the beginning of his illness and the start of treatment. His general health remained excellent, though "mooning" of the face was clearly evident. In this case the direct Race–Coombs test, previously positive, became negative during the thirteenth week of treatment whilst he was receiving A.C.T.H., though later it reverted with cortisone.

The third patient to come under treatment, a female child of 6 months, was given A.C.T.H. after a preliminary trial of transfusion. Relapse followed withdrawal

of the drug, which had been given at a dosage of 25 mg. daily, and splenectomy was undertaken during a second course of A.C.T.H. Relapse again occurred when the drug was discontinued. A third course of A.C.T.H., later changed to cortisone, was continued in gradually diminishing dosage for a further period of 14 weeks, and no ill effects have attended its final withdrawal, 28 weeks after the onset. The direct Race–Coombs test, positive at the outset, is now only weakly so.

Comment.—In this small group, one child responded after one transfusion, and another after transfusion and A.C.T.H. The other two were given intensive hormone therapy, and both were submitted to splenectomy. The relatively large requirements of A.C.T.H. made it difficult to achieve haematological response and clinical control without the production of side-effects. Undue gain in weight, mooning of the face, and glycosuria were recorded, but without biochemical or electrocardiographic evidence of electrolyte disturbance. Splenectomy proved of little benefit in the two children who relapsed after withdrawal of the drug, the operation being undertaken because of the large requirements of A.C.T.H. and the long duration of the illness. Of these two children, one appeared to recover after splenectomy performed under the protection of a second course of A.C.T.H., but relapsed on withdrawal of the drug, subsequently responding to intramuscular cortisone. The other child was operated on during a relapse, but failed to improve, the haemolytic process being ultimately controlled with cortisone. Rose and Nabarro conclude that the underlying abnormal antibody reaction can be controlled by sufficiently large doses of hormone, yet cortisone and A.C.T.H. cannot be said to displace transfusion and splenectomy in the treatment of the individual patient, both remaining as important therapeutic adjuvants.

Aplastic and Hypoplastic Anaemia

Two patients with marrow aplasia have received A.C.T.H. A man aged 27 with Hodgkin's disease, confirmed by gland biopsy, was given a long period of treatment with oral nitrogen mustard (R48), for the supply of which we are indebted to Professor Haddow. After nine months a persistent anaemia required frequent correction by blood transfusion. It seemed likely that treatment had conditioned marrow aplasia, for the anaemia was associated with thrombocytopenia and profound neutropenia. Marrow puncture gave no diagnostic information. Accordingly a trial of A.C.T.H. was made: the dosage was 100 mg. daily, reduced after eight days to 75 mg. daily. The drug was continued for 20 days (total 1.7 g.). The blood count at the start of treatment showed: Hb, 72%; W.B.C., 900 per c.mm. (60% neutrophils); and platelets, 40,000 per c.mm. No improvement occurred in the peripheral blood as a result of treatment. In the ensuing months the interval between transfusions has lengthened and the white-cell and platelet count has gradually returned to normal.

A retired policeman aged 64 had been anaemic for three years. Marrow examination at the onset in 1949 demonstrated notable reduction in the formation of erythrocytes, though the marrow was not aplastic. The diagnosis of hypersplenism was considered, but splenectomy in 1950 failed to establish a clinical cure, and since operation he had been kept alive by blood transfusions. A course of A.C.T.H., 100 mg. daily for eight days, was without effect on the anaemia and no reticulocytosis was observed. No decrease in the frequency of subsequent transfusions followed this course of treatment, which was held responsible for the recognition, three months later, of diabetes mellitus, requiring insulin. He died six months later at home, and no post-mortem examination was possible.

Comment.—In the first patient the restoration of a normal blood count was seemingly uninfluenced by A.C.T.H., the subsequent haematological improvement being more in keeping with the experience of Matthews (1950) though occurring rather less promptly, which probably reflected on the large amount of R48 previously given. In the year of observation following the course of A.C.T.H. there has been no progression of the Hodgkin's disease, which appears entirely quiescent. In the case of idiopathic aplastic anaemia A.C.T.H. had no effect on the blood condition, diabetes mellitus developing three months later as a complication of treatment.

Agranulocytosis

A patient with agranulocytosis consequent on thiouracil treatment of thyrotoxicosis was admitted as an emergency. A blood count showed 1,200 leucocytes per c.mm., with 4% neutrophils; and marrow examination demonstrated severe hypoplasia of the myeloid series. A.C.T.H., 25 mg. six-hourly, produced prompt symptomatic and haematological improvement, with myeloid hyperplasia evident at a second marrow examination on the fourth day of treatment, the peripheral blood at this time showing 70% of polymorphs in a total white-cell count of 2,900 per c.mm. Restoration to normality was complete by the seventh day, and there seemed little doubt that A.C.T.H. was the agent responsible for the swift reversal of this profound neutropenia.

A housewife aged 57 had been found to be granulocytopenic two years previously. Apart from a course of sulphonamides, given prior to recognition of the condition, no cause was evident. Treatment with haematinics had been without effect and she was subject to recurrent coliform urinary infections. The total white-cell count averaged 2,000 per c.mm., with neutrophils 10–20%. Marrow examination demonstrated a failure of maturation of the cells of the myeloid series in a quiescent marrow. Seven intravenous infusions of A.C.T.H., each of 20 mg. in 1 litre of normal saline, were given on alternate days without significant change in the peripheral white-cell count, and a seven-day course of A.C.T.H. by intramuscular injection (total 900 mg.) was similarly ineffective. Her progress has been followed for 18 months. Her health remains good, though still liable to interruption by urinary tract infection, and on one occasion by a large gluteal abscess of spontaneous origin from which *Bact. coli* was cultured. The added complication of a mild diabetes mellitus, recognized six months after the course of A.C.T.H., has been well controlled by dietary restriction of carbohydrates.

The third patient in this group, a man aged 51, first came under treatment for a left-upper-lobe pneumonia which gradually resolved with antibiotic therapy. Granulocytopenia was observed at this time, the bone marrow showing granulocytopoiesis to be arrested at the stage of transition from myeloblasts to myelocytes, the more mature forms showing heavy toxic stippling. The erythroid elements were hyperplastic in response to a moderately severe anaemia. The anaemia was corrected by blood transfusion, and the patient returned to work. His condition slowly deteriorated, with irregular pyrexia and progressive fall in the neutrophils to 7% of a leucocyte count of 2,400 per c.mm. A.C.T.H., 100 mg. daily for 16 days, caused some improvement, the white-cell count after treatment being 3,300 per c.mm., with 64% neutrophils. The diagnosis in this case remained obscure, the haematological findings being compatible with a chronic agranulocytosis or progressive marrow aplasia. Further investigation was prevented by the development of psychotic traits, the patient taking his own discharge and dying a month later at home. The possibility of tuberculosis was suggested by a chest *x*-ray examination within a month of death, which showed a diffuse mottling throughout the lung fields.

Comment.—Of three patients with agranulocytosis, an excellent response to A.C.T.H. occurred in the one in whom thiouracil was the agent responsible for the acute development of serious neutropenia. A.C.T.H. was entirely

without effect in a second case of agranulocytosis of idiopathic origin and two years' duration, and led to the later development of diabetes. In a third patient, A.C.T.H. produced a temporary improvement in the white-cell count where the cause of the granulocytopenia remained obscure.

Thrombocytopenic Purpura

Cortisone has been used in two cases. A man aged 65, with a lifelong bleeding tendency and several previous admissions for thrombocytopenia, was readmitted because of persistent epistaxis, with a platelet count of 100,000 per c.mm. and a bleeding-time of 12 minutes. Cortisone, 100 mg. daily intramuscularly, was given for five days without significant haematological response, though the bleeding stopped on the second day of treatment.

The second patient, a woman aged 39, developed thrombocytopenic purpura after a course of sodium aurothiomalate given for disseminated lupus erythematosus. The platelet count averaged 80,000 per c.mm., sternal marrow biopsy showing no evidence of aplasia or leukaemia, the megakaryocytes being normal in number and form. The spleen was not palpable. Splenectomy was done without persisting effect on the platelet count and bleeding continued, requiring frequent transfusion. Treatment with A.C.T.H., 100 mg. daily for three days followed by 50 mg. daily for two weeks, coincided with clinical improvement, and bleeding ceased shortly after the drug was discontinued, the platelet count showing little significant change. Since this time two further episodes of bleeding and purpura have necessitated her readmission, but her general condition has steadily improved and she is now well. The lupus erythematosus is quiescent.

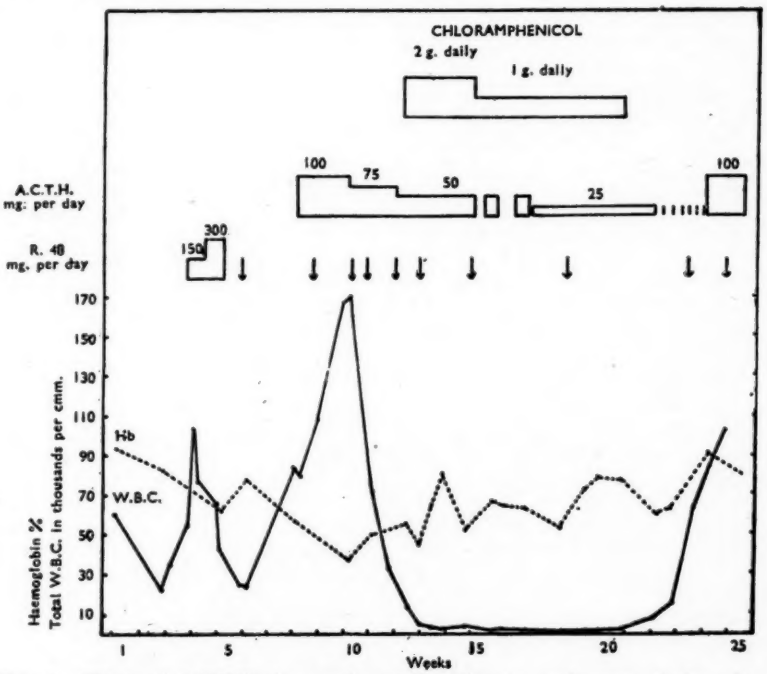

FIG. 1.—Effect of A.C.T.H. in a patient with subacute myelogenous leukaemia. Arrows indicate blood transfusions.

Comment.—In both patients clinical improvement coincided with the administration of cortisone or A.C.T.H., unaccompanied by significant haematological response.

Leukaemia

Three patients with leukaemia have been treated with A.C.T.H. The first of these, a woman aged 42, presented in an acute termination of a myeloid leukaemia with the unusual feature of extensive glandular enlargement. Three weeks previously she had completed a course of deep *x*-ray therapy. Blood examination showed 51% neutrophils, 22% metamyelocytes, and 27% myelocytes in a total white-cell count of 48,000 per c.mm. A.C.T.H. was given at a dosage of 100 mg. daily for seven days, without clinical improvement or haematological response, the peripheral blood demonstrating an increasing number of less-differentiated cells in a higher total count. Her death from cerebral haemorrhage followed shortly on the withdrawal of A.C.T.H.

Our second patient, a man aged 30, had subacute myeloid leukaemia and the clinical appearance of so-called "pseudo-scurvy." A course of R48 was discontinued on the development of skin purpura and A.C.T.H. introduced in an attempt to influence the extreme dysphagia occasioned by infiltration and oedema of the oropharynx. Symptomatic relief was rapid and striking, regression of swelling and clearing of ulceration from the mouth being associated with control of fever and a sensation of well-being that bordered on the euphoric. The total white-cell count initially increased, but later it progressively and rapidly declined to leucopenic levels, averaging 1,500–2,500 per c.mm., with neutrophils about 40–60% and lymphocytes 60–40%; immature white cells disappeared from the peripheral blood (Fig. 1). The dosage of A.C.T.H. was gradually reduced, but attempts to discontinue it entirely were met by a prompt return of fever with local and general deterioration. It appeared probable that A.C.T.H. was the agent responsible for the temporary control of the leukaemic process, though the concomitant employment of chloramphenicol may well have contributed to marrow depression—an effect reported in this country by Hawkins and Lederer (1952) and by Wolman (1952). In the fifteenth week of treatment with A.C.T.H., and some nine days after chloramphenicol had been discontinued, the peripheral blood demonstrated a return of leukaemic features, with the reappearance of primitive white cells. Thereafter deterioration was rapid, jaundice preceding death.

The third patient, a boy aged 16 with acute myeloid leukaemia, received five daily transfusions each of 25 mg. of A.C.T.H. in 1 litre of normal saline. The total white-cell count fell from 140,000 to 13,000 per c.mm. in this period, but the proportion of primitive cells remained unchanged. The later administration of folic acid antagonists clouded estimation of the therapeutic effect, but no remission followed, and the boy has since died.

Comment.—We have had no experience of the effect of cortisone and A.C.T.H. in the acute leukaemias of childhood, in which favourable results have been reported. In this small group of older patients with myeloid leukaemias the discouraging response to treatment has been in keeping with that generally recorded.

ENDOCRINE DISEASES

Exophthalmic Ophthalmoplegia

Our original report (Chandler and Hartfall, 1952) concerned the treatment with cortisone and A.C.T.H. of five patients (Cases 1–5) with this condition. Since then four more patients have been treated, without dietary regulation of sodium.

Case 6.—A woman aged 70 developed thyrotoxicosis in January, 1951. Treatment with thiouracil led to general improvement, but proptosis and chemosis became more pronounced, though unaccompanied by ophthalmoplegia. She was admitted in March, 1952, and given A.C.T.H., 100 mg. daily for 21 days, without change in the ocular condi-

tion, either subjective or objective. Her thyrotoxicosis showed no signs of settling and she was given a treatment dose of I^{131} in June, 1952. Control of thyrotoxicosis has been associated with a slow improvement in the eye signs.

Case 7.—A woman aged 25 underwent partial thyroidectomy for primary thyrotoxicosis in April, 1951. There was some post-operative increase in exophthalmos, and on admission in May, 1952, the exophthalmometer readings were R. 23 mm., L. 22½ mm. Gross nystagmus, hysterical in pattern, prevented measurement of duction movements. There was no diplopia. She gave the impression of considerable anxiety without evidence of thyrotoxicosis (B.M.R. +20%). Treatment with cortisone by mouth, 25 mg. six-hourly, was started on May 30 and continued to June 19. There was some slight subjective improvement and a minimal decrease in proptosis (R. 21 mm., L. 22½ mm. on June 19). The dosage was reduced to 50 mg. daily on July 2, and then to 25 mg. daily on July 7, and was finally discontinued after another three weeks. No further change was observed, the readings of exophthalmos in November being R. 21 mm. and L. 22 mm. The patient claims continued symptomatic relief.

Case 8.—This patient was a woman aged 50. The onset of bilateral proptosis four years previously antedated by nearly two years the clinical recognition of thyrotoxicosis. Thiouracil treatment was instituted in January, 1951, but was discontinued after five months because of leucopenia. Since this date there has been little change, either in thyroid status or in the severity of the eye signs. In August exophthalmos measured R. 22½ mm. and L. 23½ mm. There was no oedema either of lids or of conjunctivae, and the ocular movements were full. The patient was euthyroid as judged by B.M.R. and radio-iodine studies. A course of cortisone, 100 mg. daily by mouth to a total of 2 g., was entirely without effect on the eye signs, and a subsequent trial of A.C.T.H. was likewise ineffective.

Case 9.—A man aged 54 was admitted on October 19, 1952, with a short history of progressive exophthalmos, first noted in the left eye four months previously. Diplopia was experienced on upward movement, and, concomitantly with the ocular disturbance, increasing irritability and weight loss suggested a mild thyrotoxicosis, confirmed by B.M.R. (+40%) and radio-iodine studies. Examination revealed rigid proptosis (R. 24 mm., L. 27 mm.), with chemosis and conjunctival prolapse. There was gross limitation of upward movement in both eyes with paresis of left inferior oblique and left superior rectus. A course of A.C.T.H. to a total of 2 g. (100 mg. daily for 20 days) was undertaken. During the period of observation and treatment the ophthalmoplegia and area of diplopia increased, later measurement of proptosis showing R. 26 mm. and L. 28 mm.—a small deterioration.

Comment

In summary, six patients showed no improvement, yet three responded well and one dramatically. This conflict of response is reflected in the publications of other investigators, some of whom (Lederer and Hambresin, 1950; Cole, 1951) reported conspicuously favourable results.

The reasons for this remarkable disparity are not immediately obvious, though some preliminary and necessarily tentative conclusions appear to be justified.

1. Our best results were obtained with A.C.T.H. in patients whose exophthalmos was of recent origin or had suddenly and rapidly progressed. It is possible that the greater effectiveness of A.C.T.H. may be the result of the stimulation of mineral corticoid secretion and consequent local withdrawal of fluid from the orbital tissues (Campbell, 1952). Such an effect could be expected in exophthalmos of recent development only before fibrotic changes have occurred in the ocular muscles and tissues. We have previously had experience of the ability of these steroid hormones to promote a saline diuresis in certain oedematous states (notably the nephrotic syndrome), and our original investigation was framed so as to relate the sodium balance of patients with exophthalmos to the effect of treatment.

2. Those patients in whom exophthalmos and thyrotoxicosis coexist form a group of particular therapeutic difficulty. Though a treatment dose of I^{131} may prove a less drastic insult to the thyroid–pituitary relationship than partial thyroidectomy, yet in our series the control of thyrotoxicosis was the most notable feature of the treatment of two patients (Cases 1 and 5) in whom this coexisted with exophthalmos and ophthalmoplegia. This suppressive effect of the adrenal steroid hormones on thyroid function is in accord with the experience of Hill *et al.* (1950), who obtained good results in three out of six patients with uncomplicated Graves's disease. However, two patients in our series (Cases 6 and 9) showing the combination of thyrotoxicosis and exophthalmic ophthalmoplegia obtained no benefit from A.C.T.H.

3. Our experience with cortisone in patients showing exophthalmos unaccompanied by ocular muscle weakness has been entirely disappointing (Cases 6, 7, and 8), and no benefit from treatment has been observed. These patients showed only an overfilling of the orbit, presumably the effect of excess of fat.

4. Another consideration, that of dietary restriction of sodium which was enforced in our original series (Cases 2–5), cannot be discounted as a factor responsible for clinical improvement, bearing in mind the belief that oedema of the orbital tissues plays a part, at least, in the production of exophthalmos.

Simmonds's Disease

A.C.T.H. has been used in the treatment of three women with panhypopituitarism. On inquiry all gave histories typical of this disorder, dating their illness to a previous childbirth which had been attended by severe post-partum haemorrhage, following which lactation had never been established and the periods had failed to return. They had lost in energy, appetite, and variably in weight, one patient in particular presenting the picture of pituitary cachexia originally described by Simmonds (1914). Her slow deterioration over the years had been interrupted by infrequent attacks of drowsiness and coma. One such attack was observed in hospital, the patient lapsing into semi-coma with markedly cold extremities, immersion in a hot bath producing a striking but temporary improvement.

Clinical examination showed, in each, the changes of severe pituitary insufficiency. One patient was notable for the absence of mental change, preserving a bright though facile cheerfulness, in striking contrast to her physical enfeeblement. Of the others, one was deaf and apathetic, the other confused and hallucinated. The details of investigation before and during treatment are recorded in the accompanying Table. The Thorn test was normal in all, and hypoglycaemic unresponsiveness was observed in the two patients (Cases 2 and 3) in whom this investigation was made.

Treatment was by A.C.T.H. alone, and led to an improvement which was considerable in all, and dramatic in one (Case 2). It was appreciated by the patients, who without exception spoke of a feeling of strength and health, which had been absent for many years. The mental condition returned to normal in the two patients (Cases 1 and 2) in whom the symptoms of confusion and hallucination had predominated. Increase in appetite was universal, though gain in weight was not remarkable, averaging 8 lb. (3.6 kg.). All mentioned their new-found freedom from cold.

Concomitant anaemia, of normochromic type, which existed in Cases 1 and 3, did not respond to A.C.T.H., either alone or in combination with haematinics, and blood transfusion was required in Case 3 to correct the deterioration in this respect, the Hb having fallen to 49%.

Urinary excretion of 17-ketosteroids increased in all patients, particularly during the early weeks of treatment, but this was not maintained and perhaps was related to the reduction in dose of A.C.T.H. Examination of the fluid balance was remarkable for the demonstration, prior to the inception of A.C.T.H. therapy, of the small intake of water on which these patients were able to exist, the 24-hour urinary volume averaging 400–600 ml. The low level of sodium, which was a feature of the plasma chemistry of Cases 1 and 2, returned to normal and remained so under the influence of A.C.T.H. Serial E.C.G. recordings showed a parallel improvement. These patients have now returned home. Their maintenance requirements are being met by a single weekly injection of "acthar gel" 40 mg., on which

Effect of A.C.T.H. in Three Patients with Simmonds's Disease

Case	Age	Duration of History	Days from Start of A.C.T.H.	Hb %	B.M.R.	Blood Cholesterol (mg./100 ml.)	Blood Na (mg./100 ml.)	Blood K (mg./100 ml.)	17-Ks in mg./24 Hours	Fasting Blood Sugar (mg./100 ml.)	A.C.T.H. Dosage	Response
1	63	25 yrs.	0 7 20 25	84 67 	−28%	268 140	280 345 333	19·6 17·1 17·8	0·8 5·0 1·9	60 80	25 mg. I.M. b.d. 25 ,, ,, ,, 25 ,, daily 25 ,, alt. days	Excellent. Discharged home on 25th day of treatment. Maintenance requirements, acthar gel 40 units weekly
2	58	32 yrs.	0 25 47 160	91 90 	−50%	240 180 250	270 325 330	15·7 18·8 17 18	2·3 4·0 3·8 2·1	80 130	25 ,, b.d. 25 ,, daily 25 ,, alt. days 25 ,, ,, ,,	Excellent. Severely confused and hallucinated on admission. Mental condition now normal. Returned home on 51st day of treatment and is managing all housework. Continuing as an out-patient on acthar gel 40 units weekly
3	42	18 yrs.	0 18	64 49	−7%	130	332 315	21·5 16·5	1·2 3·1	70	25 ,, q.d.s. 25 ,, b.d.	Good. Previously bed-ridden, is now taking an active part in her household duties. On acthar gel 40 units weekly as an out-patient

17-Ks = Urinary 17-ketosteroid excretion.

improvement has been steadily sustained: all are leading active useful lives, managing their homes in a way previously impossible of fulfilment.

No toxic effects have been observed in this series, the appearance of oedema of feet and legs during the initial period of treatment responding to moderate salt restriction and the later reduction in A.C.T.H. dosage.

Comment.—The effect of A.C.T.H. in severe pituitary insufficiency has been studied in three patients, with a benefit from treatment so remarkable as to leave no room for doubt. In one patient (Case 2), almost moribund on admission, the effect was life-saving. They are now restored to useful domestic activity, though the glandular deficiency is such that continued maintenance treatment seems necessary.

Adrenal Hyperplasia

Cortisone has been given to four patients. Two were young women showing the syndrome of adrenal virilism, and two were children presenting as pseudo-hermaphrodites.

Adrenal Virilism

A woman aged 22 had noted rapid gain in weight and irregular menstruation for six months. Examination revealed moderate hirsutism, mooning of the face, and gross acne of the chest and back. The blood pressure was normal. The urinary excretion of 17-ketosteroids varied between 28 and 34 mg. per 24 hours, and the test for dehydroisoandrosterone was negative. Perirenal air insufflation and aortograms were thought to exclude an adrenal tumour. Total right adrenalectomy was without benefit or appreciable effect on 17-ketosteroid excretion. Two months later, left hemi-adrenalectomy was carried out under the protection of cortisone, 200 mg. being given on the day before operation, the drug being carried into the immediate post-operative period in gradually diminishing dosage. There resulted a very definite improvement in hirsuties, and the urinary excretion of 17-ketosteroids declined to an average of 6 mg. per 24 hours. Within two months, however, symptoms returned in their old severity, 17-ketosteroid excretion increasing to 15 mg. per 24 hours, and a third operation of left subtotal adrenalectomy was undertaken, the adrenal remnant being some one and half times the size of the normal gland. Five-sixths of this was removed, again under the cover of cortisone, which was given at a dosage of 50 mg. daily for two days before and for seven days after operation. The adrenal tissue removed at these successive procedures showed no histological abnormality. The further progress of this patient has been reasonably satisfactory, though a tendency to hirsutism remains.

The second patient, a woman aged 25, had been raised as a boy until the age of 9, when a large clitoris was removed. The mother noted hirsuties at this time. Menstruation later occurred only under the influence of oestrogens. She presented with typical virilism, a strong beard requiring shaving twice daily. There was no evidence in the skin or face of basophilism, and the B.P. was 190/120. Urinary excretion of 17-ketosteroids was 26.5 mg. per 24 hours. An aortogram demonstrated enlargement of both adrenal glands without evidence of tumour. Excretion of 17-ketosteroids increased to a maximum of 108 mg. per 24 hours during a period of in-patient observation. Total right adrenalectomy was followed by a course of cortisone, 50 mg. daily for 34 days, during which 17-ketosteroid excretion fell to normal, the hirsuties greatly improving. Left subtotal adrenalectomy was done five months later under the protection of a second course of cortisone, but within two months of this operation a mild Addisonian syndrome developed, with weakness, vomiting, and pigmentation. She improved with deoxycortone acetate and salt therapy, cortisone being withheld as her condition suggested functional activity of the adrenal remnant. The histological appearances were those of simple cortical hyperplasia.

Comment.—Surgical removal of hyperplastic adrenal tissue and cortisone therapy have effected a small improvement in two patients with virilism; in neither did the results appear commensurate with the risks involved, though the time of observation had admittedly been short.

Pseudo-hermaphroditism

An infant of 3 weeks presented with persistent vomiting and perineal hypospadias. The diagnosis of female pseudo-hermaphroditism was confirmed by a raised urinary 17-ketosteroid excretion of 8.2 mg. per 24 hours (normal less than 1 mg.) and the infant's inability to retain salt. Despite vomiting, the urinary excretion of salt averaged 2 g. daily on an intake of less than 0.5 g. a day. The blood sodium was 228 mg. per 100 ml., chloride 430 mg. per 100 ml., and potassium 25 mg. per 100 ml. The infant was given extra saline equivalent to 2–3 g. of salt a day, with cortisone 5 mg. intramuscularly daily. The 24-hour excretion of 17-ketosteroids fell rapidly to an average of 1–1.5 mg., but the child remained ill and miserable, passing loose offensive stools; analysis of a 24-hour specimen showing 47% of total fatty matter with trypsin present down to a dilution of 1:100. A loose cough was uninfluenced by a course of aureomycin. After four weeks, deoxycortone acetate, 2 mg. daily, was introduced and cortisone continued at a dosage of 5 mg. intramuscularly twice weekly, with some clinical improvement and restoration of the blood sodium and chloride levels to normal. The improvement was short-lived, the child dying from bronchopneumonia in the eighteenth week. At necropsy the suprarenal glands were greatly enlarged (each weighing 10.4 g.) and showed a pale hyperplastic cortex. Histological examination revealed fibrocystic disease of the pancreas.

The second patient, first seen aged 3 years 3 months, had hitherto been reared as a boy. He was of slender build with girlish facies, showing a perineal hypospadias flanked on either side by gonadal sacs containing no testes. Over these sacs and the top of the phallus there was a quantity of black hair, suggesting a masculinizing process in a female.

This was confirmed by hormone estimations on the urine: 17-ketosteroids, 16.6 mg. per 24 hours; dehydroisoandrosterone, negative; follicle-stimulating hormone, 17 units. These results suggested bilateral diffuse hypertrophy of the adrenal cortex, though the amount of follicle-stimulating hormone, not usually present at this age, raised the possibility of primary pituitary dysfunction. The patient's bone age was between 5 and 6 years. Laparotomy a year later demonstrated female internal organs, biopsy from the right ovary showing normal ovarian tissue.

Cortisone therapy was started in July, 1952, the child being then almost 5 years old. The dosage was 50 mg. daily for three weeks, reduced to 25 mg. daily for a further four weeks, thereafter continued at 75 mg. and 100 mg. twice weekly. The 24-hour excretion of 17-ketosteroids, which had averaged 18–19 mg. per 24 hours prior to cortisone therapy, was controlled in the succeeding months at 4–6 mg. per 24 hours. Little objective change has so far occurred, but the child is well and happy, conforming easily to feminine outlook.

MISCELLANEOUS CONDITIONS

Cirrhosis with Portal Hypertension

Our experience of the treatment of this syndrome with A.C.T.H. has been limited to two patients in whom hepatic fibrosis had occasioned portal hypertension with frequent episodes of gastro-intestinal bleeding. Previous reports (Bongiovanni and Eisenmenger, 1951) of the effect of A.C.T.H. in cirrhotic subjects have stressed the risk to those patients whose liver function is seriously impaired. In others, certain benefit seems to have attended treatment, though evidence of the specific nature of the response is lacking.

A man aged 35 developed cirrhosis consequent on homologous serum jaundice. Three attacks of haematemesis at six-monthly intervals brought him under our observation, when, in addition to the finding of splenomegaly, extensive oesophageal varices were visible on barium examination and confirmed at oesophagoscopy. Measurement of oesophageal varix pressure (Mr. Allison) showed an excess over systemic venous pressure of 140 mm. H_2O. A course of A.C.T.H. was given over 39 days of study (total 2.5 g.). Day-to-day variation in dosage was determined by the patient's response, particularly in relation to fluid and salt retention and also by the levels of blood sugar. Fluid retention was easily induced—far more readily than has been our experience in other conditions with similar dosage. The details of treatment and investigation are shown in Fig. 2. Serial estimations of plasma chemistry showed a progressive and sustained improvement in liver function with final return to normality. Direct measurement of portal hypertension gave equivocal results. By the fifth week of treatment the pressures in the portal and systemic systems were equal, but this second measurement coincided in time with the period of maximum fluid retention and systemic venous pressure was notably raised. Six months later, measurement showed that the difference in pressure between the two systems was as before treatment. Treatment occasioned some improvement in general health, and in the eight months since A.C.T.H. was discontinued the improvement, both clinical and biochemical, has persisted without recurrence of bleeding.

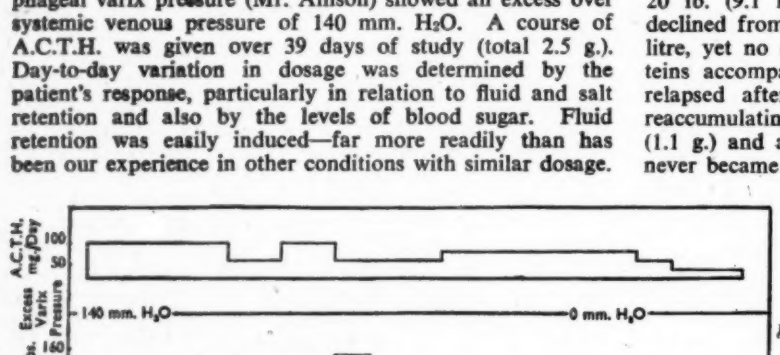

FIG. 2.—Effect of A.C.T.H. on a patient with hepatic cirrhosis and portal hypertension. Note initial rapid increase in weight, with equalization of portal and systemic venous pressures at a time of maximum fluid retention, and improvement in the levels and ratio of plasma proteins.

A man aged 36 had survived numerous attacks of haematemesis and melaena as well as the operations of splenectomy and oesophageal devascularization, both without benefit. This patient suffered a recurrence of bleeding whilst under treatment, and has recently reported a further attack of melaena. A.C.T.H. has contributed nothing to this man's rehabilitation.

Comment.—This small experience suggests that A.C.T.H. has no certain place in the present admittedly unsatisfactory attack on the problem of portal hypertension, though it may remain a valuable therapeutic adjuvant in the treatment of cirrhosis.

Nephrotic Syndrome

We have had experience of the paradoxical diuretic power of these drugs in two patients whose presentation conformed to that described by Ellis (1942) as type II nephritis.

A woman aged 48 developed the characteristic triad of oedema, albuminuria, and hypoproteinaemia following on the employment of sodium aurothiomalate for a polyarthritis of rheumatoid type. Yet the time interval of nearly 12 months was such that the aetiological role of gold was of questionable significance. This patient received cortisone at a dosage of 100 mg. intramuscularly daily for six weeks (total 4.3 g.) and by the fourth week of treatment had lost 20 lb. (9.1 kg.) and was clear of oedema. Proteinuria declined from 7–8 g. per litre to an average of 1–2 g. per litre, yet no change in the level and ratio of plasma proteins accompanied this clinical improvement. She slowly relapsed after cortisone had been discontinued, oedema reaccumulating, uninfluenced by a 10-day course of A.C.T.H. (1.1 g.) and a final short course of cortisone, though she never became so waterlogged as on admission. Renal function was unchanged as judged by clearance tests, and the patient was normotensive throughout.

Our second patient, a girl of 15 years, came under observation in March, 1951, when for two months she had noticed swelling of the feet and legs, unaccompanied by haematuria. She was found to have gross albuminuria and a B.P. of 180/120. Since this time, oedema had fluctuated but never remitted. Renal function was adequate; the plasma chemistry demonstrated reversal of the albumin/globulin ratio. In March, 1952, no improvement having followed the adoption of orthodox dietary measures, A.C.T.H. was started at a dosage of 25 mg. intramuscularly six-hourly and continued for 17 days (total 1.7 g.), the patient being placed on a diet providing a constant daily intake of sodium. During the administration of A.C.T.H. she gained weight steadily, oedema sensibly increasing in a period of negative sodium balance (Fig. 3). Cessation of A.C.T.H. was followed by a profound saline diuresis over 10 days, when the patient lost 15 lb. (6.8 kg.) in weight, oedema clearing entirely. Albuminuria

diminished slightly and the level of blood cholesterol fell from 350 to 170 mg. per 100 ml. This patient's progress has been observed for 12 months, and neither increase in weight nor return of oedema has occurred. Hypertension remains unaltered, and renal function is adequate. No significant change was noted in the level of plasma proteins during the time of in-patient observation, but in the succeeding months the trend of the plasma chemistry has shown an encouraging progress to normality.

Comment.—Two patients with a nephrotic syndrome have been treated with cortisone and A.C.T.H. The first patient went into remission whilst under treatment with cortisone, decrease in albuminuria and diuresis occurring simultaneously. Partial relapse followed the withdrawal of cortisone. In a second patient, treated with A.C.T.H., the diuresis was observed immediately after withdrawal of the drug and continued for 10 days. In this case the remission induced by treatment has lasted for 12 months. It seems clear from these observations that A.C.T.H. and cortisone are capable of exerting profound effects on electrolyte metabolism. More doubtful, however, is the possibility that the underlying disease process has been radically altered. This favourable response to cortisone and A.C.T.H. compares with other clinical reports of the effect of induced malaria (Gairdner, 1952), and the natural remissions sometimes observed following measles, for these may well represent the common results of adrenal activation by stress. Whatever the precise mechanism, these effects of the adrenal steroids in nephrotic disease provide interesting problems in fundamental physiology.

Asthma

The dramatic relief afforded to patients with bronchial asthma, and particularly those in status asthmaticus, by cortisone and A.C.T.H. is generally known. We have had the opportunity of observing their effects in nine patients, all of them subjects of severe chronic asthma, for whom emergency hospital admission had been requested after the usual remedies had failed.

Three women in their fifties obtained rapid relief from a single intravenous infusion of normal saline to which 20 mg. of A.C.T.H. had been added. These drips were allowed to run for 12 hours, when symptomatic benefit was such that treatment could confidently be continued by more orthodox means.

A woman aged 45, admitted desperately ill in intractable status asthmaticus, did not respond to A.C.T.H. by intravenous infusion and died on the second day. Post-mortem examination demonstrated almost solid plugging of the air passages by thick mucoid material, a mechanical obstruction to respiration which only bronchoscopic aspiration might have relieved.

Two patients have been treated with cortisone by inhalation, 5 mg. of the standard preparation being made up into 2 ml. with normal saline and administered at two-hourly intervals. The response of both lacked the dramatic quality attending the use of intravenous A.C.T.H., but was judged by the patients themselves to provide more rapid and lasting improvement than they had obtained in previous attacks of similar severity.

Two patients have received cortisone by intramuscular injection. A housewife aged 59 derived no benefit from 100 mg. of drug given daily for five days. The other, a woman of 25 in status asthmaticus, made an excellent response to 50 mg. given thrice weekly for five doses, treatment being continued at 50 mg. twice weekly for a further fortnight. The remission in this patient lasted until her return home one week later.

Though not directly touching on the therapy of the asthmatic attack, cortisone has been used in a case of allergic asthma in which orthodox desensitization had been abandoned because of the production of severe asthma. It was found possible to complete desensitization under the protection of cortisone, 25 mg. twice weekly, and since its completion the patient, a man aged 40, has remained free of attacks.

Comment.—We have confirmed the beneficial effects of cortisone and A.C.T.H. in seven of nine patients with severe bronchial asthma. The intravenous infusion of A.C.T.H. in normal saline seems to offer the best prospect of rapid symptomatic relief, and, together with the topical administration of cortisone by inhalation, allows of considerable economy in prescribing. The remissions induced by these forms of treatment average one to two months, probably differing little from the duration of freedom afforded by the more usual forms of treatment.

Summary

The effect of cortisone and A.C.T.H. in non-rheumatic diseases has been studied in 43 patients.

Fourteen patients with disorders of the blood have been observed. A favourable response occurred in three children with acute acquired haemolytic anaemia, and in thrombocytopenic purpura apparent clinical benefit resulted in the two patients treated. No effects were produced in aplastic anaemia, though one patient with acute agranulocytosis from thiouracil made a good response. The effect of A.C.T.H. in leukaemia was at best temporary. This small experience suggests that, apart from acquired haemolytic anaemia and some cases of purpura, cortisone and A.C.T.H. have little place in the treatment of blood disorders.

Sixteen patients with disorders of endocrine function have been studied. Of nine patients with exophthalmic ophthalmoplegia, only three responded well, the best results being obtained with A.C.T.H. in those examples of recent onset or rapid progression. Three patients with Simmonds's disease have made a dramatic and sustained improvement on A.C.T.H. Two patients showing the virilizing effects of adrenal hyperplasia have been

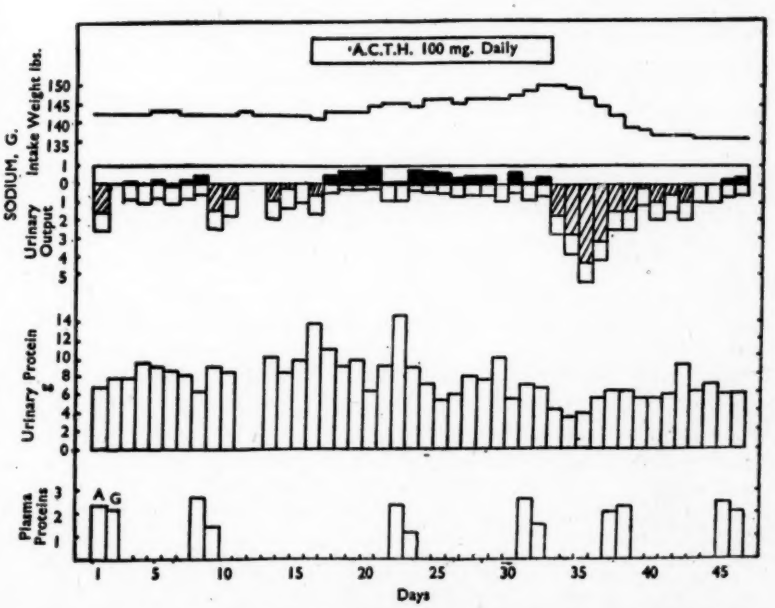

FIG. 3.—Effect of A.C.T.H. in a patient with nephrotic syndrome. Black areas, positive sodium balance; hatched areas, negative sodium balance. Note rapid loss of weight and saline diuresis when A.C.T.H. was discontinued. The levels and ratio of plasma proteins show no persisting improvement.

treated by adrenalectomy and cortisone : in neither did the results obtained appear to justify the risks involved. 17-ketosteroid excretion was controlled in two pseudo-hermaphrodites by the use of cortisone.

The beneficial effect of cortisone and A.C.T.H. in asthma has been confirmed. The use of A.C.T.H. by intravenous drip and of cortisone by inhalation usually brought prompt improvement and was an important economy in prescribing. In two patients with nephrosis a considerable diuresis attended treatment, and in one of them the remission obtained has lasted more than a year. There is no evidence that A.C.T.H. influences portal hypertension accompanying cirrhosis, though apparent clinical benefit occurred in one patient.

We are grateful to the physicians and surgeons of the General Infirmary at Leeds and the Hospital Cortisone Committee, who have allowed us to publish details of patients under their care. We are indebted to the Medical Research Council for the cortisone used in the treatment of exophthalmic ophthalmoplegia and to Armour Laboratories for a supply of acthar gel.

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DEVELOPMENTAL DYSARTHRIA

BY

MURIEL MORLEY, B.Sc., F.C.S.T.

DONALD COURT, M.D., M.R.C.P.

AND

HENRY MILLER, M.D., F.R.C.P., D.P.M.

(From the Children's Department, Royal Victoria Infirmary, Newcastle-upon-Tyne, and the Department of Child Health, Durham University)

In 1950 we advocated a simple classification of speech disorders in childhood (Miller and Morley, 1950). This had grown naturally from our work and was conceived within the framework of accepted neurological terminology. The five broad categories of deafness, defective articulation or dysarthria, retarded development of language or dysphasia, dyslalia, and stammering, with their main subdivisions, are presented again, as follows :

Disorders from Deafness
1. Congenital nerve deafness:
   (*a*) Severe for all frequencies.
   (*b*) Partial, or high-frequency deafness.
2. Acquired nerve deafness.

Dysarthria
1. Due to local anatomical lesions of the speech organs.
2. Dysarthria with neurological signs of cerebral disease or maldevelopment.
3. Dysarthria unassociated with abnormal neurological signs elsewhere.

Dysphasia
1. Mainly expressive dysphasia.
2. Mainly receptive dysphasia:
   (*a*) Dyslexia.
   (*b*) ? Congenital auditory imperception.
3. Delayed development of speech or global dysphasia.

Dyslalia
Transient defects of consonant substitution and omission.

Stammering.

Continuing experience has confirmed the value of this classification in assessing the prognosis and designing the treatment of the individual child. In the past two years we have given particular attention to the problem of dysarthria, which is, to us, slow and clumsy articulation arising from dysfunction of the muscles used in speech. The association with cerebral palsy in all its forms is well known. A group of children, however, presented with dysarthria as the only disorder without detectable neurological abnormality in any other part of the body. It is this isolated form of dysarthria which is the subject of this paper. The literature on the subject is scanty, but suggests that the condition is uncommon. As we have studied 18 affected children over a period of four years we realize that it occurs more often than we suspected, and should be more widely recognized. We shall first describe four children whose cases illustrate the clinical patterns we have seen, and then consider the nature of the condition and its differentiation from other forms of defective articulation.

Clinical Patterns in Developmental Dysarthria

Case 1 : Dysarthria with Clumsy Movements of Lips, Tongue, and Palate.—This boy is now 7 years 9 months old. He is the second child in the family, was born before the arrival of the nurse, and weighed 12 lb. 10 oz. (5.7 kg.). He breathed and cried immediately after birth, was sucessfully breast-fed for seven months, and was walking on his first birthday. Words were first used between 12 and 18 months and sentences from 2 years onwards. On his first visit at the age of 5 his mother complained that "he dribbled when he was excited, sucked instead of chewing his food, and could not talk properly." Though rather nervous, he co-operated well and his I.Q. on the Drever Collins scale was 111. No abnormality could be found in the nervous system except that speech was slow and clumsy, the tongue bunched and writhed on lateral movement, and the palate moved to the right. During speech the lips, tongue, and soft palate moved in an awkward and uncoordinated fashion. Two years after the beginning of treatment he could repeat all consonant sounds except "s," and speech was intelligible when spoken slowly, though some final consonants were still omitted. Although it may be some years before he speaks easily, and still longer before speech is satisfactory under stress, it seems likely that this boy will eventually achieve normal speech.

Case 2 : Dysarthria with Clumsy Movement of the Soft Palate.—This 15-year-old girl is the second of four children. There is a history of language delay in her father until the age of 7 and of an unspecified speech difficulty in a cousin persisting into adult life. She was born normally and weighed 11 lb. 4 oz. (5.1 kg.). Her mother does not remember the child's early years very clearly, but she did not take the breast or bottle well and was slow in gaining weight. She was walking just before her first birthday. She was almost completely silent until 2, and then words came slowly. When first seen at 11 years she was a pleasant sensible girl with no evident disease of the nervous system apart from a tight soft palate which bunched up in the centre but did not contract at the sides. There was no sign of a submucous cleft. Speech was nasal in character. Consonants were weak or were omitted, and attempts to coordinate the use of vowels and consonants produced a

severe dysphonia. She ceased to attend for treatment, and four years later there had been little improvement in articulation. At 15 her reading age was 12 years 8 months and the palatal movements were unchanged. During a further course of treatment a transient dysphonia recurred, but four months later she had made considerable progress, and speech was normal except for an occasional audible nasopharyngeal leak, due to incoordination, when hurried. Her I.Q. on the Wechsler-Bellevue scale was 96, and her school report speaks of a "co-operative well-behaved girl, who, without outstanding qualities, had reached a fairly good standard of general attainment."

Case 3: Dysarthria with Clumsy Movements of the Tongue.—This boy, now aged 6 years 9 months, is a second child. Birth was normal and he weighed 10 lb. (4.5 kg.). There was no difficulty with feeding or swallowing, and he walked at the age of 14 months. His father had had a speech difficulty which persisted into school life. This boy began to use words at a year, and sentences followed very soon after. When first seen at the age of 5½ he was a well-developed boy of high intelligence, with an I.Q. by the Alexander performance test of 150. The nervous system was normal apart from a thick and clumsy tongue with poor lateral movement. Speech, however, was unintelligible. Sixteen months later speech was much improved, especially in formal rhymes and repetition, but was still clumsy when he attempted spontaneous conversation. The abnormal appearance and behaviour of the tongue was unchanged. We have regarded this boy as a case of dysarthria uncomplicated by dysphasia, in whom treatment has been facilitated by high intelligence.

Case 4: Dysarthria Without Apparent Clumsiness of Lips, Tongue, or Palate.—This boy is now 9 years old. The fourth child, he was born prematurely and weighed only 3 lb. (1.36 kg.). His behaviour during the first few weeks is not fully known, but at one stage "he was not expected to live." He did not dribble excessively and there was no apparent difficulty in swallowing. He was walking at the age of 15 months, and has always been a good runner. He did not begin to use words in any quantity until 2. When first seen at 6 he was a friendly active boy with no abnormality in the nervous system apart from defective speech. This was fluent, but intelligible only to his parents. The tongue, lips, and palate were normal in appearance and movement. Although at first he was thought to be an example of simple dyslalia, the failure to respond quickly to treatment suggested a more complex disorder of speech. He had difficulty in imitating and using consonant sounds, and was helped considerably by watching the therapist's articulation. When imitation of consonants was possible in isolation and in single words, he had exceptional difficulty in incorporating consonants correctly in speech. Two and a half years later his articulation was still defective, and, with increasing awareness of this, he had become more cautious, often repeating words silently before speaking. His I.Q. on the Wechsler-Bellevue scale was 113.

General Features of Developmental Dysarthria

Of the 18 children with this condition 12 were boys and 6 were girls. They have been observed for periods varying from 1 to 6 years, and their present ages range from 6 to 17. They come from all social classes and cover the full range of normal intelligence. The four children described earlier in this paper illustrate the clinical variations we have seen, and we shall now comment briefly on some common or frequently associated features.

Family Tendency.—There was an impressive history of speech defect in parents, siblings, or close relations in 10 of our families. Although we were unable to interview all the affected members personally, it was clear from the accounts given by the parents that the difficulty had been considerable and had continued in some instances into adult life.

Birth Injury.—In only three cases was birth injury suspected from the history, and in none was the evidence convincing. That this is unlikely to play an important part is borne out by the position of the affected children in the family. Only one was first-born, eleven were second, and six were third or later births.

Prematurity.—One of the 18 children was born prematurely—an incidence of prematurity similar to that for Newcastle-upon-Tyne in recent years (F. J. W. Miller, 1948).

Emotional Disturbance.—The majority of these children developed normally and happily in spite of their handicap. In two there were intermittent emotional difficulties which were not apparently related to their speech, while in a third, growing awareness of his defective articulation produced a reticence and hesitation which was absent in the earlier years. We have no grounds for believing that psychogenic factors play any important part in this group of disorders.

Appearance and Movements of the Lips, Tongue, and Palate.—Abnormal appearance and abnormal voluntary movements of the lips, tongue, or palate were present in 12 of the 18 children, and were the only abnormal physical signs apart from defective speech. The tongue is often thick and firm, with slow clumsy movements from side to side and difficulty or inability in pointing or turning it upwards over the lip. The upper lip also may give the impression of being tight and inflexible during speech, and the soft palate may show poor voluntary movement or fail to produce effective closure of the nasopharynx.

In the remaining six children, otherwise clinically similar, movements of the lips, tongue, and palate appeared normal on voluntary movements carried out at the examiner's request, but clumsy and awkward when the children attempted the more complex and rapid movements of articulation. We have regarded such cases as possible examples of "dyspraxic dysarthria" or "articulatory dyspraxia."

Associated Disorders of Language.—In nine of the children there was also delay in the development of language. The extent of this difficulty varied considerably. In one child the delayed appearance of words was followed by a limited vocabulary, dyslexia, and dysgraphia throughout school life. In three others, although there was no delay in starting to talk, dyslexia was still present at 9 and 12 years of age. In the remaining five children, words and sentences appeared later than the normal time, but three of these had a generous vocabulary by the age of 6. Dysphasia is a common associate of dysarthria in evident cerebral palsy: if these cases of isolated dysarthria are, as we believe, due to a structural brain defect, the frequency of associated dysphasia is not surprising.

Prognosis.—The less severely affected child, particularly when endowed with high intelligence, can make good progress and achieve almost normal speech by the age of 7 or soon after. The commoner experience is for progress in developmental dysarthria, even with faithful treatment, to be slow, and for the defect to reappear whenever there is emotional stress or excitement. In some children traces of the defect will linger on into the late teens, and in one family not included in the present account four members are still unintelligible at the ages of 54, 61, 69, and 72 years.

Aetiology

There are many features which suggest that these cases are developmental in origin, and we are certain that they are structurally and not psychogenically determined. The family history of speech disorders, the frequency of abnormal movements of the lips, tongue, and palate, the close similarity of these isolated dysarthrias to the dysarthria of cerebral palsy, and the steady but slow improvement in response to time and training are factors which speak strongly in favour of an organic basis.

The natural history of this condition is that of a defect of maturation. The disability shows neither the intermittency and tendency to recurrence of the emotionally determined speech difficulty such as stammering nor the rapid response to treatment with which we are familiar in those cases of temporary consonant substitution to which we have limited our use of the term "dyslalia." In our view the lesion in developmental dysarthria is analogous to that of spastic diplegia in nature if not in situation. The site of the lesion is problematical. It is certainly suprabulbar, and would seem to depend on a focal cerebral dysgenesis essentially similar to but more limited in extent than that with which we are familiar in spastic diplegia. It is for these reasons that we have adopted the term "developmental dysarthria," first suggested to us by Dr. C. Worster Drought (personal communication, 1952), to describe these cases and as the title of the present paper.

Diagnosis

Developmental dysarthria must be separated on the one hand from the dysarthria of cerebral palsy, and on the other from severe dyslalia. Where the dysarthria is part of a persisting minimal spastic diplegia recognition requires nothing more than careful physical examination. The differentiation of developmental dysarthria from the group of articulatory defects for which we reserve the term "dyslalia" is, however, not always easy and may be impossible without testing the response to treatment; but in most instances the distinction can be made on the basis of a careful history and examination.

In developmental dysarthria speech is slow and clumsy and, in severe examples, punctuated by explosive words and phrases. The child is unable to imitate speech quickly and easily, and the chief defect of pronunciation is omission with or without substitution of consonants. Many such children show the characteristic appearances and defective movements of tongue and palate already described and identical with those seen in cerebral palsy. In some children, however, the movements are apparently normal except when the muscles are used in articulation. The specific clumsiness evident under such circumstances appears to depend on a disturbance of function, an articulatory dyspraxia, arising at a higher level of the nervous system than is involved in cases where neuromuscular function is visibly abnormal. In a considerable proportion of dysarthric children there is also a history of slow development of language and a poor vocabulary with persisting difficulty in reading.

In the child with severe dyslalia, on the other hand, language develops at the normal time and speech is fluent even if unintelligible. There is no abnormality in the movements of the lips, tongue, or palate, and the defect of pronunciation is largely one of multiple consonant substitutions. The most striking difference between the two conditions lies in the response to treatment. Whereas in dysarthria recovery is slow, in dyslalia normal speech should be reached within three to twelve months from the start of consistent treatment. That these two broad groups of articulatory defects exist is obvious in everyday experience, and, whereas developmental dysarthria is structurally determined, dyslalia would appear to be a functional disorder of speech which responds quickly to guidance and treatment.

Summary

Within the general context of dysarthria in childhood we wish to draw attention to a group of children in whom dysarthria is unassociated with any neuromuscular abnormality elsewhere. The clinical features suggest that this is a structurally determined condition, for which the term "developmental dysarthria" would be fitting.

We have seen a smaller number of children also covered by this term in whom we suspect that the defect is essentially an articulatory dyspraxia.

The condition may or may not be associated with delayed development of language and difficulty in reading.

The outlook varies with the severity of the defect and the intelligence of the child; response to consistent treatment is usually slow, and occasionally the difficulty persists into adult life.

We value the opportunity which our colleagues have given us to study these children, and would like to express our thanks to Sir James Spence for his encouragement and advice. We are also grateful to Mr. R. F. Garside, of the department of psychological medicine, who assessed the children's mental development.

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ESTIMATION OF INTRINSIC FACTOR OF CASTLE BY USE OF RADIOACTIVE VITAMIN B_{12}

BY

SHEILA T. CALLENDER, M.D., M.R.C.P.

ADAM TURNBULL, B.M., M.R.C.P.

AND

GYOICHI WAKISAKA,* M.D.Kyoto

(From the Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford)

Pernicious anaemia is attributed to the failure of absorption of vitamin B_{12} in the absence of the secretion by the stomach of the substance known as intrinsic factor (Castle, 1951). The preparation of pure vitamin B_{12} labelled with radioactive cobalt (Co^{60}) (Chaiet, Rosenblum, and Woodbury, 1950) presented a method of assessing the absorption of orally administered vitamin B_{12} and thus of detecting intrinsic factor activity. Heinle and his colleagues (1952) estimated the radioactivity appearing in the faeces after an oral dose of 0.5 μg. of radioactive vitamin B_{12}. They found that between 72 and 96% of the radioactivity in this test dose was recovered from the faeces of four patients with pernicious anaemia unless a source of intrinsic factor was given simultaneously, when the recovery was less than 30%. In two normal subjects on three occasions they recovered no radioactivity, but on one occasion in one subject, when he was convalescing from pneumonia, 42% was recovered. A. D. Welch (1952, personal communication) indicated the difficulties encountered in these early experiments owing to the low specific activity (60 μc./mg.) of the radioactive vitamin B_{12} used.

Using radioactive vitamin B_{12} of higher specific activity (245 μc./mg.), Meyer (1953) recovered from the faeces between 89 and 99% of a 1-μg. test dose in four patients with pernicious anaemia and between 15 and 59% in seven control subjects. Significant reduction in the recovery of radioactivity, however, did not occur consistently when a source of intrinsic factor was given with the radioactive vitamin B_{12}.

The preparation by Lester Smith (1952) of radioactive vitamin B_{12} of high specific activity (420 μc./mg.) has enabled us to extend these experiments.

*In receipt of a British Council Scholarship.

Method

Vitamin B_{12} labelled with radioactive cobalt (Co^{60}) was given to a group of control patients with normal haematological findings and to patients with pernicious anaemia, and the radioactivity appearing in the faeces was measured.

A standard dose of 0.5 μg. of radioactive vitamin B_{12} containing approximately 0.2 μc. of radioactivity was given by mouth in about 100 ml. of water. No food was allowed after 10 p.m. on the previous evening and for two hours after the dose had been taken, but the patient was allowed one cup of tea first thing in the morning (at least two hours before the dose was given); apart from this the patient took a normal diet. The stools were passed direct into glass containers and were collected until at least one contained less than 1% of the radioactivity of the test dose. No aperients were allowed for 24 hours before or after the test dose. Repeated tests were made on most of the patients in order to diminish the possibility of error due to incomplete collection of the stools. If this was suspected the test was discounted.

Each stool specimen was transferred quantitatively to a domestic electric mixer with enough water to allow the faeces to be blended to a uniform homogeneous suspension, which was then transferred quantitatively to a beaker and weighed. After further mixing an aliquot was transferred to a stoppered glass bottle and set aside for estimation of the contained radioactivity.

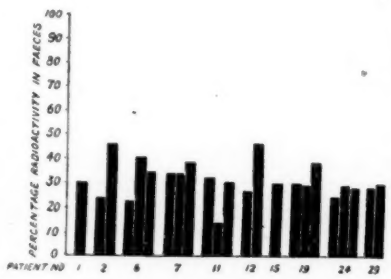

FIG. 1.—Recovery of radioactivity from faeces after an oral dose of 0.5 μg. of radioactive vitamin B_{12} in 10 control patients.

The radioactivity of the specimens was estimated by means of a scintillation counter comprising a crystal of sodium iodide 2½ in. (6.3 cm.) in diameter and a photomultiplier and scaling unit supplied by A.E.R.E., Harwell. Each specimen was weighed out into a 30 by 50 mm. glass weighing - bottle, which was stood on a thin brass tray over the crystal. The tray had raised edges, which ensured that each bottle was held in the same place.

Counting was carried out with a photomultiplier voltage of 2 kV and a discriminator bias of 12 volts. Under these conditions background counts of between 120 and 160 a minute were obtained, the efficiency of the counter for Co^{60} being approximately 8%. It was found that the empty weighing-bottles gave counts of 10 to 30 a minute above background, and so each bottle was first counted empty to obtain the true background.

Then 50 g. of each of the faecal suspensions was weighed out in duplicate and the radioactivity counted. Since the specific gravity of the stools is approximately one, differences in volume were negligible. The counts obtained with the specimens were compared with that of 50 ml. of a standard solution containing one-tenth of a test dose. Each specimen was counted in duplicate for five minutes and an average taken of the two results. If, however, these differed by more than 2% (when expressed as a percentage of the total dose administered) further aliquots were counted.

Results

Normals

Radioactive vitamin B_{12} was given to 10 patients who were in hospital for various complaints but who were considered to be haematologically normal, except for patient No. 7, who had a moderate hypochromic anaemia (haemoglobin 9.8 g.%) following the nailing of a fractured femoral neck and who was receiving ferrous sulphate. These patients were mostly in the same age group as our patients with pernicious anaemia. Their diagnoses and the results obtained with radioactive vitamin B_{12} are shown in Table I and Fig. 1.

These results show that in the normal patient between 20 and 40% of the radioactivity in a test dose of 0.5 μg. of radioactive vitamin B_{12} usually appears in the faeces. In the third test on patient No. 2 the recovery was 60%. He was at the time suffering from an upper respiratory infection. Recoveries of between 45 and 60% have also been

TABLE I.—*Radioactivity in Faeces After Oral Dose* (0.5 μg.) *of Radioactive Vitamin* B_{12} *in* 10 *Control Subjects*

Patient	Age	Sex	Diagnosis	Date	Total Radioactivity in Faeces as Percentage of Dose
1	46	F	Benign hypertension	4/11/52	30
2	64	M	Duodenal ulcer	18/11/52	24
				7/4/53	45
				13/4/53	60*
6	57	F	Fractured neck of femur	7/1/53	22
				16/1/53	40
				23/1/53	34
7	65	F	Fractured neck of femur	7/1/53	34
			Hypochromic anaemia	16/1/53	34
			Mild senile parkinsonism	23/1/53	38
11	78	F	Fractured neck of femur	6/2/53	32
			Mild cerebral arterio-sclerosis	16/2/53	14
				27/2/53	30
12	82	F	Fractured neck of femur	6/2/53	26
			Osteoarthritis of hips	10/3/53	45
15	65	F	Peripheral neuritis	3/3/53	30
19	45	M	Duodenal ulcer	28/2/53	30
				9/3/53	29
				16/3/53	37
24	50	F	Benign hypertension	21/3/53	25
				31/3/53	29
				8/4/53	28
29	56	M	Gastric ulcer	14/4/53	28
				20/4/53	30

* See text.

TABLE II.—*Radioactivity in Faeces After Oral Dose* (0.5 μg.) *of Radioactive Vitamin* B_{12} *in* 13 *Patients with Pernicious Anaemia*

Patient	Age	Sex	Duration of Disease	Date	Total Radioactivity in Faeces as Percentage of Dose
4	62	F	2 years	29/11/52	90
				30/12/52	95
				12/1/53	91
	55	F	19 ,,	31/12/52	87
				13/1/53	86
				16/2/53	90
8	66	M	27 ,,	10/1/53	92
				21/1/53	91
				6/2/53	99
13	69	M	2½ ,,	7/2/53	92
				16/5/53	76
16	80	F	21 ,,	17/2/53	95
				9/3/53	91
20	67	F	3 months	6/3/53	84
				12/3/53	79
21	72	F	19 years	10/3/53	86
				1/4/53	98
22	76	M	17 ,,	17/3/53	85
				31/3/53	79
				7/4/53	81
23	61	M	2 ,,	20/3/53	81
				7/4/53	79
28	70	M	3 ,,	10/4/53	79
				4/5/53	99
				11/5/53	101
30	74	F	1 year	28/4/53	95
				27/5/53	91
31	73	F	12 years	8/5/53	90
32	60	M	19 ,,	26/4/53	90

obtained in four other patients during the course of infections. It seems that infections interfere with the test, and we have therefore excluded from the figures the results of the third test on No. 2.

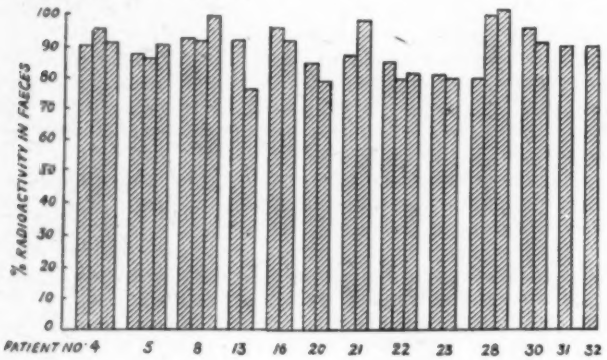

FIG. 2.—Recovery of radioactivity from faeces after an oral dose of 0.5 μg. of radioactive vitamin B_{12} in 13 patients with pernicious anaemia.

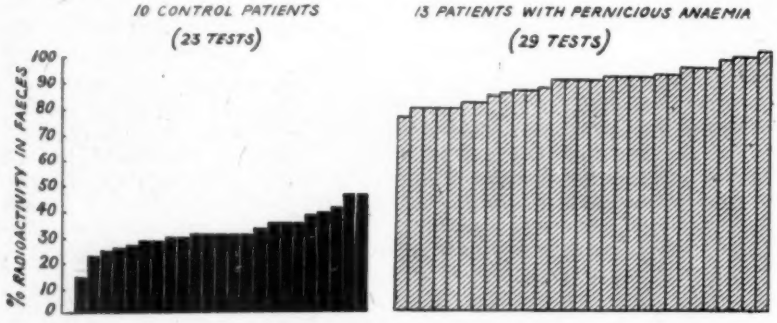

FIG. 3.—Comparison of recoveries of radioactivity from faeces after oral doses of 0.5 μg. of radioactive vitamin B_{12} in 10 control patients and 13 patients with pernicious anaemia.

TABLE III.—*Effect on the Recovery of Radioactivity from the Faeces of Giving a Source of Intrinsic Factor with an Oral Dose of Radioactive Vitamin B_{12} in Eight Patients with Pernicious Anaemia*

Patient	Date	Material Given	Total Radioactivity in Faeces as Percentage of Dose of B_{12} Given
20	6/3/53	0·5 μg. B_{12}	84
	12/3/53	"	79
	18/3/53	" and 100 ml. human gastric juice (Pool A)	34
	24/3/53	" " " "	32
22	17/3/53	"	85
	24/3/53	" " " (Pool B)	59
	31/3/53	"	79
	7/4/53	"	81
	14/4/53	" " " (Pool C)	54
23	20/3/53	"	81
	27/3/53	" " " (Pool B)	57
	7/4/53	"	79
	14/4/53	" " " (Pool C)	52
13	7/2/53	"	92
	14/2/53	" and 100 ml. gastric mucosal extract (T2)	53
	21/2/53	" " " (T4)	43
	16/5/53	"	76
21	10/3/53	"	86
	10/4/53	" " " (T7)	44
	1/5/53	"	98
30	28/4/53	"	95
	18/5/53	" and 10 mg. " fraction B "	60
	27/5/53	"	91
31	8/5/53	"	90
	15/5/53	" " " "	49
32	26/4/53	"	90
	27/5/53	" " " "	66

Pernicious Anaemia

Radioactive vitamin B_{12} was given to 13 patients who had had classical pernicious anaemia for various periods. All except patients Nos. 4 and 20 were in good remission under treatment with vitamin B_{12} (" cytamen "). Nos. 4 and 20 have both responded excellently to injections of vitamin B_{12} started after their first test with radioactive vitamin B_{12} had been completed.

The results obtained are shown in Table II and Fig. 2. In these patients between 76 and 101% of the radioactivity in the test dose was recovered from the faeces. Fig. 3 summarizes the results obtained in the normal patients and those with pernicious anaemia.

It might be argued that the apparent failure of absorption of the radioactive vitamin B_{12} in these treated patients with pernicious anaemia was due to their tissues being saturated with vitamin B_{12}. The test was therefore repeated, giving a source of intrinsic factor together with the vitamin B_{12}. Patients Nos. 20, 22, and 23 received radioactive vitamin B_{12} mixed with 100 ml. of pooled neutralized normal human gastric juice. Nos. 13 and 21 received as their source of intrinsic factor watery extracts of gastric mucosa. Nos. 30, 31, and 32 were given radioactive vitamin B_{12} with 10 mg. of an ammonium-sulphate-precipitated fraction of hog stomach mucosa (" fraction B ") prepared by the method of Prusoff *et al.* (1950).

The results of these experiments are shown in Table III and Fig. 4. It will be seen that the amount of radioactivity recovered from the faeces was diminished whenever a source of intrinsic factor was given, although it seems that the various preparations differed in potency.

Discussion

Our results confirm those of Heinle and his colleagues (1952) in that we find that there is a gross difference between the percentage of radioactivity of 0.5 μg. of labelled vitamin B_{12} recovered from the faeces in normal subjects and in patients with pernicious anaemia. However, the addition of preparations containing intrinsic factor to the test dose reduced the faecal recovery of radioactivity considerably less than in their experiments. This difference is probably in part due to the greater accuracy resulting from the use of radioactive vitamin B_{12} of higher specific activity, and in part to variations in potency of the sources of intrinsic factor.

It is interesting that even the normal subjects in our series did not absorb completely this small amount of vitamin B_{12}. It must be emphasized that it is the Co^{60} which is being estimated, and that this is not necessarily still in a molecule

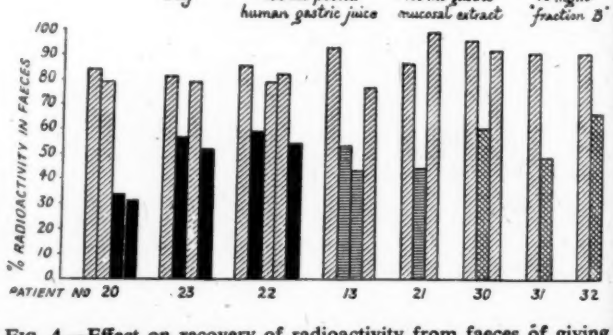
0·5μg B12 only
0·5μg B12 + 100 ml pooled human gastric juice
0·5μg B12 + 100 ml gastric mucosal extract
0·5μg B12 + 10 mgm "fraction B"
% RADIOACTIVITY IN FAECES
PATIENT NO 20 23 22 13 21 30 31 32

FIG. 4.—Effect on recovery of radioactivity from faeces of giving a source of intrinsic factor with an oral dose of 0.5 μg. of radioactive vitamin B_{12} in eight patients with pernicious anaemia.

of vitamin B_{12}. Moreover, if some vitamin B_{12} is destroyed in the gastro-intestinal tract with the liberation of free ions of cobalt, it is possible that some of the latter might be absorbed as such.

Some of our patients with pernicious anaemia seem to have absorbed a fraction of the radioactive vitamin B_{12}, and this may indicate, as Goldhamer (1936) first suggested, that some patients with pernicious anaemia secrete traces of intrinsic factor. The significance of our figures depends chiefly on the accuracy of the stool collections. Experience in this department with radioactive iron (Fe^{55}), which was given by mouth and recovered from the red blood corpuscles and from the faeces, supports the view that incompleteness of stool collection is unlikely to account for all the radioactivity which was not recovered.

It appears that this technique offers a simple measure of intrinsic factor activity in the patient, and that it may also be used to assay preparations for their content of intrinsic factor. It has many advantages over the clinical assay, which requires patients with pernicious anaemia in relapse, but it has the disadvantage that it is an indirect test which depends on the absorptive power of the gastro-intestinal tract at the time at which the test dose is given. Preliminary evidence of the effect of infections suggests that the absorption of vitamin B_{12} is easily interfered with in the normal subject. Further investigation of this point is in progress.

Summary

The absorption of vitamin B_{12} has been assessed by measuring the radioactivity in the faeces after an oral dose of 0.5 μg. of vitamin B_{12} labelled with Co^{60}.

In 10 patients with normal haematological findings a mean of 31.0% (standard deviation, 6.9%) of the radioactivity in the test dose was recovered from the faeces. In 13 patients with pernicious anaemia a mean of 88.7% (standard deviation, 6.8%) was recovered.

Sources of intrinsic factor given with radioactive vitamin B_{12} to patients with pernicious anaemia reduced greatly the percentage of the test dose recovered.

It is a pleasure to express our thanks to Professor L. J. Witts for allowing us to study patients under his care and for his constant help and encouragement; Dr. L. Z. Cosin for allowing us to study patients under his care in the Cowley Road Hospital; Dr. Lester Smith, of Glaxo, Ltd., for supplies of radioactive vitamin B_{12}; Dr. Arnold Welch for the "fraction B"; Dr. W. B. Taylor for the gastric mucosal extracts; Mr. Ray Oliver for advice and assistance in the radioactivity measurements; Dr. John Badenoch for help and advice; and Miss Barbara Hunt for technical assistance. This work was in part supported by a grant to Professor L. J. Witts from the Medical Research Council.

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The World Health Organization has recently issued the report of the discussion at the third European Seminar for Sanitary Engineers which was held in London from October 27 to November 1, 1952. The book is entitled *Design and Operation of Septic Tanks*, and among topics discussed are the treatment of small sewage plants, the design of small sewage works, and comparative studies of septic tanks. It is published in the Monograph Series (No. 18), price 7s. 6d., and is obtainable through H.M. Stationery Office, London, or direct from the Sales Section, Palais des Nations, Geneva.

RESEARCHES IN AETIOLOGY OF NON-SPECIFIC URETHRITIS*

BY

R. R. WILLCOX, M.D.

St. Mary's Hospital, London, W.2

General Observations

Non-specific urethritis (N.S.U.) is one of the most perplexing conditions encountered in the British venereal diseases clinic to-day. When complicated by Reiter's syndrome its disabling powers are considerable. In the clinics of England and Wales in 1951 there were 10,794 cases of non-specific urethritis, as compared with 14,975 male cases of gonorrhoea.

Although the condition is usually acquired venereally in the male, it is possible that the female may on occasion be infected non-venereally, which would explain the slight non-venereal bias. Thus in 100 cases of gonorrhoea the last sexual risk had been a casual exposure in 60%, whereas in 100 cases of non-specific urethritis the comparable figure was only 40%. Also, of 640 subjects of non-specific urethritis studied 35.3% were married, whereas of 603 male subjects of gonorrhoea only 25% were married. Persons suffering from non-specific urethritis were of slightly older age groups than those with gonorrhoea, and more likely to be in a "white collar" occupation—both observations perhaps being reflections of the marital status.

Some observers (for example, Coutts of Chile) have suggested that the practice of oral and/or anal coitus may frequently be responsible for the transmission of non-specific urethritis. This would not appear to be the case in Great Britain, for such practices were admitted by only 6% of 50 patients with non-specific urethritis so questioned, as against 9% of 100 other patients attending the venereal diseases clinic during the same period.

The incubation period of non-specific urethritis is often longer than that of gonorrhoea. Of two groups, each of 150 cases, 52% of patients with non-specific urethritis had incubation periods of over seven days, as compared with only 32% (in itself a high figure) in the case of patients with gonorrhoea.

Ignoring established rare causes, the following have variously been regarded as possibly responsible for the bulk of cases: (1) bacteria; (2) pleuropneumonia-like organisms; (3) trichomonads; (4) spirochaetes; and (5) a virus. This study was limited mainly to a consideration of bacterial and viral causes.

Bacterial Urethritis

It has for some time been fashionable to divide non-specific urethritis into bacterial and abacterial urethritis, depending on whether bacteria are seen in the urethral smears. Some 301 urethral cultures were made at King Edward VII Hospital, Windsor (pathologist, E. Sayle), on consecutive patients with non-specific urethritis, before and after treatment with the orally administered antibiotics, and on controls. As a result it is considered that "bacterial urethritis" is not a common entity and that the bacteria found are usually commensals (Table I).

*Being a summary of the report presented to the British Medical Association at the conclusion of the term of office as Insole Research Scholar.

TABLE I.—*Urethral Cultures*

Organisms	Controls (105 Cultures)		Non-specific Urethritis Cases			
			Before Treatment (81 Cultures)		After Treatment (69 Cultures)	
	No.	%	No.	%	No.	%
S. albus	72	68·6	66	81·4	55	79·7
Bact. coli ..	22	21·0	16	19·7	9	13·0
Diphtheroids ..	19	18·1	26	32·1	27	39·1
Saprophytes ..	8	7·6	4	4·9	9	13·0
S. aureus ..	4	3·8	1	1·2	—	—
Monilia	3	2·8	1	1·2	1	1·4
B. proteus ..	—	—	—	—	1	1·4
Enterococci ..	—	—	2	2·5	—	—
Streptococci ..	—	—	1	1·2	2	2·9
Sterile	2	1·9	1	1·2	3	4·3

Viral Urethritis

Attempts were made, by different means, to ascertain whether there was any cross-reaction in the skin or blood of patients with non-specific urethritis to antigens of various viruses of the psittacosis/lymphogranuloma venereum/trachoma group. A study was also made of Giemsa-stained urethral scrapings, and animal and egg studies were undertaken.

Skin Tests

In all, some 234 tests were performed—175 for lymphogranuloma venereum, 28 for psittacosis, and 31 for cat-scratch fever. Omitting the later tests, the results of the first tests are shown in Table II.

TABLE II.—*Skin Tests*

	Tested	Negative	Doubtful	Positive	% Positive
Lymphogranuloma venereum (1):					
N.S.U. cases ..	84	63	10	11	13·1
Controls	62	53	6	3	4·8
Psittacosis (2):					
N.S.U. cases ..	17	15	2	—	—
Controls	11	11	—	—	—
Cat-scratch fever (3):					
N.S.U. cases ..	16	12	2	2	12·5
Controls	12	12	—	—	—

Antigens kindly supplied by: (1) E. R. Squibb and Sons, International Corporation, New York ("lygranum") and Virus Reference Laboratory, Colindale; (2) Virus Reference Laboratory, Colindale (courtesy of Dr. A. D. Macrae); and (3) Professor P. Mollaret, Hôpital St. Bernhard, Paris, and Virus Reference Laboratory, Colindale (courtesy of Dr. H. J. Bensted).

Thus the skin tests for psittacosis gave negative results. In the series tested, however, some positive readings were obtained with cat-scratch antigen in patients with non-specific urethritis, but not in controls. Also a somewhat higher incidence of positive readings to the skin test for lymphogranuloma venereum was noted in patients with non-specific urethritis than in controls. This aspect of the problem, therefore, would merit further attention.

Serum Tests

A total of 412 complement-fixation tests for lymphogranuloma venereum (L.G.V.), on sera from 275 persons, were made by Dr. A. D. Macrae, of the Virus Reference Laboratory, Colindale. A further 323 complement-fixation tests for enzootic abortion in ewes (E.A.E.), on sera from 250 persons, were performed by Dr. J. T. Stamp, of the Edinburgh and East Scotland College of Agriculture, Edinburgh. The latter veterinary disease is considered to be caused by a virus of the lymphogranuloma venereum/psittacosis/trachoma group.

The results of these tests are being recorded fully elsewhere, but are summarized in Table III.

In view of these findings and the results of serial tests performed on some cases, it was not thought that there was any relationship between the results of either test with non-specific urethritis sera. There was, however, close agreement between the results of the two tests on 263 parallel specimens of sera (Table IV).

TABLE III.—*Serum Tests (First Tests Only)*

	Tested	Negative	Doubtful	Positive	% Positive
Lymphogranuloma venereum:					
N.S.U. cases ..	141	122	13	6	4·3
Controls	132	120	9	3	2·3
Enzootic abortion in ewes:					
N.S.U. cases ..	123	113	6	4	3·2
Controls	127	118	4	5	3·9

TABLE IV.—*Comparison of L.G.V. and E.A.E. Tests*

Titres	1/10 or Below	1/20	1/4 or Over	Total E.A.E. Tests
1/4 or below ..	218	15	—	233
1/8	1	10	8	19
1/16 or over ..	1	3	7	11
Total L.G.V. tests	220	28	15	263

Giemsa-stained Urethral Scrapings

As the so-called virus of non-specific urethritis has not yet been successfully passaged in animals or eggs, the evidence for or against its existence has had to depend upon the presence or absence of inclusion bodies in Giemsa-stained urethral scrapings.

Some 1,463 Giemsa-stained urethral scrapings, taken from patients with non-specific urethritis, their female consorts, or from controls, were examined at the laboratories of the School of Pharmacy, London, under the supervision of Dr. G. M. Findlay until his death in March, 1952, his technician being Miss E. M. Howard. Through the courtesy of Professor G. A. H. Buttle, Miss Howard's services were made available after that date so that the work could be completed.

In order to determine the significance, or otherwise, of the various bodies seen, in due course the findings were classified as blue or red "colonies" (being granular bodies varying from 1–6 μ in diameter) and blue or red granules. The incidence of these various bodies in urethral scrapings was compared in male patients with non-specific urethritis before treatment, after successful treatment with one of the orally administered antibiotics, and after unsuccessful treatment (Table V).

TABLE V.—*Incidence of Various Bodies in Giemsa-stained Urethral Scrapings from Male Patients with Non-specific Urethritis*

	Before Treatment (206 Cases)		After Successful Treatment (182 Scrapings)		After Unsuccessful Treatment (103 Scrapings)	
	No.	%	No.	%	No.	%
Blue colonies ..	71	34·5	18	9·9	23	22·3
Red ,, ..	17	8·3	15	8·2	6	5·8
Blue granules ..	36	17·5	15	8·2	17	16·5
Red ,, ..	38	18·4	42	23·1	24	23·3
Nil	78	37·9	115	63·2	50	48·5

The fact that the incidence of red colonies and red granules was unaffected by treatment, successful or unsuccessful, appeared at once to exclude these as possessing no significance. On the other hand, the incidence of both the blue colonies and blue granules fell markedly after successful treatment with the orally administered antibiotics, but remained high when the treatment was unsuccessful. Moreover, at the time of actual re-treatment given to 42 cases the incidence of blue colonies was 30.9% and of blue granules 23.8%.

A group of 80 controls was also studied. These consisted of 12 specimens of non-urethral pus, urethral scrapings from 18 normal males, from 13 patients attending the clinic on account of fear of venereal disease, from 17 patients with syphilis, and from 20 patients with non-syphilitic genital lesions (for example, warts, genital herpes, etc.). In only two (2.5%) were blue colonies, and in only one (1.25%) were blue granules discovered. Up to this point, therefore, the material showed promise so far as correlation between the blue colonies and blue granules and the activity of non-specific urethritis was concerned.

However, it was appreciated that the control scrapings so far studied were in the main taken from dry urethrae, whereas those from non-specific urethritis cases were from wet urethrae. A further control series, this time of 108 cases of gonorrhoea treated at varying periods of time previously with penicillin, was therefore taken. In these, 15 (13.9%) showed blue granules and, as this incidence was almost as high as in the untreated non-specific urethritis cases, these, too, had to be discounted. The incidence of blue colonies, however, was 14.8%, still very substantially below the 34.5% found in the patients with untreated non-specific urethritis.

But when the gonorrhoea cases were arranged according to the length of time which had elapsed from the giving of the penicillin until the taking of the scraping it was noted that at one to three days after injection the incidence of blue colonies was 21.7%. This figure was not far removed from the 27.6% incidence of these bodies two to seven days after the beginning of the treatment of non-specific urethritis with one of the orally administered antibiotics (Table VI).

TABLE VI.—*Incidence of Blue Colonies in Gonorrhoea Cases*

Time Since Treatment	Cases	Blue Colonies	%
Untreated	23	2	8·7
1–3 days	46	10	21·7
4–7 ,, ...	24	4	16·6
Over 7 days	15	—	—
Total	108	16	14·8

It would seem that the blue colonies were but products of inflammation, since in both gonorrhoea and non-specific urethritis their incidence decreased as the urethra became drier. That they were seen relatively seldom in the discharges of untreated gonorrhoea was probably connected with the essentially high leucocytic and low epithelial count of the specimens at this stage. It was therefore regretfully concluded that none of the bodies studied in this investigation were involved in the causation of non-specific urethritis.

[A consideration of smears from female cases is omitted from this summary and will appear in the paper being prepared with Miss E. M. Howard.]

Animal Experiments

Attempts to transmit the virus of non-specific urethritis into baboons, guinea-pigs, mice, and eggs were made in the laboratories of the School of Pharmacy.

A sustained attempt to passage the virus into the lungs of mice was a failure. The haemorrhagic lesions which were seen in a number of the 1,735 mice used in these experiments proved not to be related to the disease. Limited attempts at intracerebral inoculation into mice, subcutaneous inoculation into guinea-pigs, and conjunctival instillation, urethral inoculations, and inoculation into the knee-joints of baboons, likewise failed to give any clear-cut evidence of transmission. Attempts to transmit the virus in the chorio-allantoic membranes of eggs also failed; these latter experiments, which involved about 100 eggs, were confused by the presence of other bodies which bore a resemblance to those seen in the urethral scrapings of patients suffering from non-specific urethritis.

Summary and Conclusions

When compared with gonorrhoea, non-specific urethritis was apparently more frequently contracted from regular consorts, indicating a possible non-venereal bias in its aetiology.

In the urethritis group more patients were married, they tended to be older in age, and they were more likely to have achieved " white-collar " status than those of the gonorrhoea group.

There was no evidence to suggest that the practice of buccal or anal coitus was commonly responsible for the transmission of non-specific urethritis.

The disease tended to have a longer incubation period than gonorrhoea.

A study of 301 urethral cultures taken from patients with non-specific urethritis before and after treatment, and from controls, suggested that the so-called " bacterial urethritis " was uncommon.

The results of 412 complement-fixation tests for lymphogranuloma venereum and 323 complement-fixation tests for enzootic abortion in ewes showed nothing distinctive between sera from patients with non-specific urethritis and from controls.

A study of 234 skin tests for lymphogranuloma venereum, psittacosis, and cat-scratch fever, on the other hand, showed more positive readings in non-specific urethritis cases than in controls, and this aspect of the problem therefore merits further attention.

From the examination of 1,463 Giemsa-stained urethral scrapings it was considered that the bodies seen were products of inflammation and unconnected with the virus of non-specific urethritis. Thus, if inclusion bodies sometimes seen in these scrapings are responsible for the isolated case, the causative organism cannot be seen in the majority.

Attempts to passage the virus into the lungs of mice (1,735 mice being used in these experiments), mouse-brains, guinea-pigs, and into the conjunctiva, knee-joint, and urethra of baboons were also unsuccessful.

The " virus " of non-specific urethritis has not been isolated, and remains to be discovered.

The World Health Organization has recently published in pamphlet form a survey of modern legislation relating to nursing. The aim of the survey, it is stated, was to examine the extent to which legislation has established a system of control over the organization and practice of nursing and to indicate the new problems caused by the introduction of the auxiliary and specialized nurse. The survey reviews the laws of 22 countries. It notes the dichotomy of nursing laws: on the one hand, permissive laws which do not restrict the practice of nursing, but which give official recognition in the form of legislation to trained nurses, and thereby differentiate the qualified from the unqualified; and, on the other hand, mandatory laws which safeguard the health of the community by prohibiting the unqualified from practising, and which consequently need to define nursing. There is a general lack of precision in the definition of nursing functions, and the survey remarks that nursing, unlike midwifery and dentistry, defies precise legal definition, and consequently the professional nurse is not always provided with sufficient protection in the exercise of her calling. In recent years the shortage of nurses has become acute all over the world, and is mirrored to-day in the increasing number of laws being enacted in relation to auxiliary nursing staff and male nurses.

A SURVEY OF PATIENTS IN TWELVE MENTAL DEFICIENCY INSTITUTIONS

BY

N. O'CONNOR, M.A., Ph.D.

AND

J. TIZARD, M.A., B.Litt., Ph.D.

Medical Research Council Unit for Research in Occupational Adaptation

During the months of November and December, 1951, and January and February, 1952, we carried out a survey of a 5% sample of patients in mental deficiency institutions in the counties of London, Kent, and Surrey. The survey was concerned primarily with factual information relevant to the patients' occupational potentialities and behaviour, but, in addition, opinions on conduct were obtained. Some of the questions relating to conduct were included at the suggestion of Dr. R. F. Tredgold, regional psychiatrist to the South-East Metropolitan Region, to whom a preliminary draft of the proposed investigation was shown. A clinical classification of the patients, following A. F. Tredgold's (1947) system, which was obtained from medical officers at the time of the investigation will be discussed elsewhere.

A list of questions asked is given in summary form in the Appendix. By no means all the information obtained has been summarized in this paper, and anyone interested in other aspects of the survey is invited to get in touch with us.

Population and Sample

The population from which the 5% sample was drawn consisted of patients in all hospitals in the counties of Kent, London, and Surrey which had been classified by the Board of Control (1946) as certified institutions or institutions approved under Section 37 of the Mental Deficiency Acts. Approximately 100 patients housed in five approved homes in Surrey and Kent were excluded from the survey. The survey covered all other institutions in the selected area.

The size of the sample by hospitals is given in Table I. The population from which the sample was drawn consisted of approximately 11,850 patients, nearly one-quarter of the total number of institutional defectives in England and Wales. It should be noted that only patients certified under the Mental Deficiency Laws were included. In the case of Leavesden Hospital, for example, approximately one-third of the patients were either senile or for other reasons not certified under the Mental Deficiency Acts.

TABLE I.—*Hospitals and Institutions Visited, with Size of Sample, by Sex*

Hospital	Male	Female	Total
Botleys Park	43	37	80
Darenth Park	61	40	101
Farmfield	12	—	12
Fountain Hospital	15	17	32
Leavesden Hospital	33	40	73
Leybourne Grange Colony	28	35	63
Leytonstone House Hospital	1	17	18
Manor Hospital	36	39	75
Princess Christian's Farm Colony	4	6	10
Royal Earlswood Institution	19	11	30
St. Lawrence's Hospital	49	42	91
St. Teresa's Home	—	7	7
Total	301	291	592

Method

The physician or lay superintendent of each hospital was written to for permission to undertake the survey. They were told the purpose of the investigation and a copy of the questions to be asked was sent to them. Permission was obtained in all cases—indeed, the assistance given us at all hospitals was most generous. In each hospital the sample was selected by drawing every twentieth name from a nominal role of patients on the books, listed alphabetically, the first name to be selected being determined by lot from the first twenty names in the book. Case records and orders were examined. Additional information was obtained by questioning senior members of the nursing staff. The clinical classification was obtained subsequently from the medical staff. Patients between 16 and 29 years of age who were classified as feeble-minded and were not on licence or on leave were tested by the investigators on the progressive matrices test, in groups, but without a time limit. Between one and three days were spent at each hospital. The coded information was punched on Hollerith cards and machine-sorted.

Distribution of Patients by Sex, Age, and Grade

The distribution of patients by age, sex, and grade is given in Table II—43 (8%) were admitted under Sections 8 or 9 of the Mental Deficiency Acts, and 435 under Section 6. or other section. The data in Table II have been arranged so that the number of adults and children appear separately.

Children formed 12.33% of the patients, the majority of them being of low grade. (The Report of the Ministry of Health for the year 1949 gives the proportion of children in institutions in England and Wales as 12%, which agrees with the figure obtained in the survey.) There were 43% more males than females among the children. In Table III is given the percentage of adult patients by grade and age. The most recent report by the hospital authorities to the Board of Control was consulted in order to determine the grade of each patient.

Of the adults, 58% were classified as feeble-minded. Most of these were under 50 years of age.

TABLE II.—*Distribution of Patients by Sex, Age, and Grade*

Age	Male				Female				Totals			
	0	1	2	T	0	1	2	T	0	1	2	T
0–4	2	4	0	6	1	4	0	5	3	8	0	11
5–9	5	12	3	20	5	6	2	13	10	18	5	33
10–14	4	6	3	13	2	5	2	9	6	11	5	22
15	0	3	1	4	1	2	0	3	1	5	1	7
Total (children)	11	25	7	43	9	17	4	30	20	42	11	73
16–19	1	12	17	30	1	9	13	23	2	21	30	53
20–29	3	33	42	78	4	27	30	61	7	60	72	139
30–39	2	24	37	63	2	17	39	58	4	41	76	121
40–49	1	15	38	54	0	26	41	67	1	41	79	121
50+	0	13	20	33	1	29	22	52	1	42	42	85
Total (adults)	7	97	154	258	8	108	145	261	15	205	299	519
Total	18	122	161	301	17	125	149	291	35	247	310	592

0=Idiot. 1=Imbecile. 2=Feeble-minded person. T=Total.
Age is given as from last birthday. The number of patients aged 15 years is given separately in order that the number of children (aged 0–15) and of adults (age 16+) can be calculated.

TABLE III.—*Percentage of All Adult Patients (519) by Age and Grade*

Age	Grade			Total
	0	1	2	
16–29	2	15	20	37
30–39	1	8	15	24
40–49	—	8	15	23
50+	—	8	8	16
Total	3	39	58	100

Distribution of Patients by Type of Nursing Needed and Behaviour

There were 26 male patients and 28 female patients on resident licence from the institutions (8.6% of male patients and 9.6% of females). In addition 21 patients (16 males and 5 females) were on daily licence. The distribution of patients by sex, grade, and type of nursing needed is shown in Table IV.

TABLE IV.—*Number of Patients by Grade and Type of Nursing Needed (on Day of Survey)*

	Grade			Total
	0	1	2	
Chronic sick	1	9	11	21
Temporarily in hospital	0	3	4	7
Cot and chair cases	12	10	3	25
Low-grade ambulant	13	74	14	101
Open wards	0	75	154	229
Locked wards ("special supervision")	8	72	62	142
Hostel	0	0	6	6
On leave	0	0	1	1
Absconded	0	0	6	6
Resident licence	1	4	49	54
Total	35	247	310	592

Supplementary questions added something to the picture so far as behaviour was concerned. Thus only one male and one female patient had attempted suicide during the previous year; 12 (2%) had been charged with stealing; 55 (9%) had had one or more clashes with staff or patients serious enough to be recorded in case notes; 18 (3%) had absconded. Ten (3.8%) of the female patients had been pregnant or had had V.D. at some time in their lives, and 16 (5.8%) of the male patients had histories of homosexuality, indecent assault, or indecent exposure. Some of the incidents listed as indecent assault in case papers or orders were of a trivial character and had occurred many years previously. Seventy-seven patients (13%) were doubly incontinent, and 27 (5%) enuretic; 68 patients (11.5%) suffered from epilepsy, 17 being severe cases (suffering grand mal attacks once a fortnight or more), 14 moderate, and 37 mild. Numerous other patients were recorded on case sheets as being epileptic, but had had no attacks during the last year or, in some cases, at any time during their stay in hospital.

There were marked differences in the proportion of patients in different hospitals who were in locked wards. No doubt the type of patient was in part responsible for this, but hospital policies appeared also to differ. Of the 538 resident patients, 75 (13%) left the hospital grounds once or more on day parole during the month preceding the date of the survey (29 females, 46 males). During the previous year 76 male patients and 47 female patients (25% and 16% respectively) went on leave. Over two-thirds of these patients were on leave for less than three weeks.

Rewards to Patients

The "wages," or rewards, given to patients varied somewhat from hospital to hospital. For low-grade patients rewards consisted of sweets or cigarettes. High-grade patients usually had rewards paid partly in kind, partly in cash. The figures given in Table V refer to the cash value of the rewards, whether or not the patients received money, tokens to be exchanged at the canteen, or actual goods.

TABLE V.—*Cash Value of Rewards of Pocket Money Paid During Week of Survey to Patients Resident in Hospital*

Value in Shillings	No. of Patients	Per Cent of Total
1 or less	225	42
2	77	14
3	91	17
4	54	10
5	34	6
6–10	34	6
11–15	5	1
16+	10	2
Not ascertained	8	2
Total	538*	100

Total amount disbursed to 530 patients, £70 18s. 6d.
* Total excludes 54 patients on resident licence.

For patients not on either daily or resident licence the rewards represented total earnings. Those on licence, however, earned wages which were often in excess of the amount of pocket money allowed them. (Additional amounts, when deductions have been made for board and lodgings, are credited to patients' accounts.) Hospital policies differed in the extent to which they allowed patients on licence control over their own affairs, and wages earned by patients on licence, as well as the amount of money or goods they were given to spend or use during the week of the survey, also varied greatly. Those employed in factories and as labourers earned higher wages than those engaged in domestic service. Table VI gives the length of time patients had been on licence.

TABLE VI.—*Duration of Licence of 54 Patients out of Hospital at Time of Survey*

Period on Licence	Daily Licence			Resident Licence		
	Male	Female	Total	Male	Female	Total
Less than 3 months	1	0	1	5	2	7
3–6 months	1	0	1	4	5	9
6–12 ,,	0	0	0	4	5	9
1–2 years	4	0	4	6	8	14
2–5 ,,	6	0	6	5	5	10
More than 5 years	1	1	2	2	3	5
No information	3	4	7	0	0	0
Total	16	5	21	26	28	54

Occupations of Patients

The numbers of patients employed on different types of jobs both inside and outside the hospitals are given in Table VII. About 40% of those on licence were employed in domestic service of one sort or another. Only one hospital made a practice of sending defectives to factory work. Surprisingly few patients were employed on farms or gardens—possibly the sample of defectives on licence was too small to enable us to generalize about the kind of jobs done by patients on licence.

TABLE VII.—*Occupation of Patients During Week of Survey*

Type of Occupation	Patients Working in Hospital				On Licence		
	Grade			Total	Daily	Resident	Total
	0	1	2				
Farm or garden	0	9	19	28	6	2	8
Domestic service in hospital	0	8	27	35	0	6	6
Other domestic work (private, hotel, or kitchen)	0	0	3	3	5	22	27
Labouring	0	6	4	10	5	4	9
Factory or laundry	0	8	11	19	2	6	8
Messenger or van boy, shop assistant	0	0	7	7	3	2	5
School or occupation centre	4	19	10	33	0	1	1
Occupational therapy	0	19	20	39	0	0	0
Ward work	0	57	54	111	0	0	0
Hospital workshop	0	16	51	67	0	0	0
No information	0	0	9	9	0	6	6
Unemployable	30	101	25	156	0	5	5
	34	243	240	517	21	54	75

Intelligence of Patients Classified as Feeble-minded

As mentioned above, patients between 16 and 30 years of age who were resident in hospital and available at the time of the inquiry, and who were classified as feeble-minded, were given the group matrices test, using an untimed procedure. The distribution of *raw* scores is given in Table VIII. The numbers are small—25 males and 24

TABLE VIII.—*Distribution of Matrices Raw Scores* for Sample of 49 Patients Tested*

Raw Score*	Males	Females
0–9	2	1
10–19	9	11
20–29	5	6
30–39	8	4
40+	1	2
Total	25	24
$\bar{X}$	23·9	21·4
S	10·4	10·0

* For subjects between 20 and 30 years of age a raw score of 23 points is approximately equal to an I.Q. of 74 on a test whose mean is 100; S.D. = 16 points. For an unselected adult population 20–30 years of age the mean raw score on this test = 44 points; S.D. = 10 points.

females—and little reliance could be placed on the findings in the absence of other data. However, the results for male patients agree very closely with those obtained from testing 360 patients at Darenth Park, Harperbury, and the Manor Hospitals (Tizard and O'Connor, 1952). There is thus a considerable amount of evidence to support the conclusion, at least so far as male patients are concerned, that the mean I.Q. on this test of young adult patients classified as feeble-minded is about 74 or 75 points. The mean for females may be somewhat lower. As has been shown elsewhere (Tizard, 1950) norms for the progressive matrices test agree closely with those obtained from other tests more commonly used with defectives. Hence, if these findings are valid over the country as a whole, more than half of the adults classified as feeble-minded in mental deficiency institutions have I.Q.s of over 70 points.

Summary

A survey, based on case records, was made of a 5% sample of nearly 12,000 patients in twelve mental deficiency hospitals in the Home Counties, representing nearly one-quarter of the total number of mental defectives in institutions in England and Wales.

Over half the patients were found to have been classified as feeble-minded. Less than 5% were idiots and just over 40% imbeciles.

Intelligence quotients, measured by the progressive matrices test, in those feeble-minded patients between 16 and 29 years of age who were available, indicated, in conformity with a previous finding, that the average intelligence quotient of young adult feeble-minded defectives in hospitals near London is above 70.

Half the patients did not need special nursing or supervision; a further 24%, while needing no special nursing, were thought to be in need of close supervision.

One patient in eight was on daily licence or resident licence. Only one hospital sent patients out to factory work. Rewards to patients averaged between 2s. and 3s. for the week of the survey, 56% of the sample receiving less than 2s. and 13% more than 5s.

General behaviour of the resident patients was apparently good. Sexual perversion, pregnancy, or venereal disease was recorded in approximately 5%. Three per cent. of the patients in the sample had absconded at least once during the preceding twelve months.

Our thanks are due to the hospital authorities of the 12 hospitals and institutions visited for their kindness in allowing us to carry out the survey, and for their great assistance to us, usually at considerable inconvenience to themselves. Dr. J. M. Crawford, Dr. L. T. Hilliard, Dr. J. K. Collier Laing, Dr. Vera Norris, and Dr. R. F. Tredgold gave advice on questions to be included and treatment of results. We are indebted to Mr. J. G. F. Singleton for carrying out the Hollerith work.

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APPENDIX

Survey of Patients in Institutions in London, Kent, and Surrey. Information Obtained

1. Hospital.
2. Sex of patients.
3. Number.
4. Date of order.
5. Years in present hospital.
6. Section of the Act under which certified.
7. Age in years last birthday.
8. Grade (taken from last report to Board of Control).
9. Last I.Q. on case paper.
10. Test used to obtain last I.Q.
11. Type of nursing needed—as in Table IV of text.
12. Occupation.
13. Pocket money during previous week.
14. Paroles during previous month.
15. Number of visits per year.
16. Whether or not relatives were living.
17. Days' leave during past year.
18. Number of times absconded during past year.
19. Attempts at suicide during past year.
20. Times caught stealing during past year.
21. Clashes with patients or staff during past year.
22. Homosexual behaviour—any history of.
23. Indecent assault—any history of.
24. V.D. or pregnancy—any history of.
25. Behaviour with patients—rating.
26. Behaviour with staff—rating.
27. Epilepsy—recorded as in text.
28. Incontinence.
29. Whether or not on daily licence at any time.
30. Type of work done.
31. Reason for failure in past, if any
32. Resident licence.
33. To whom licensed.
34. Type of work.
35. Failure ?
36. Duration of licence.
37. Wages on licence.
38. Matrices raw score.
39. Clinical classification.

Professor D. R. MacCalman, Nuffield Professor of Psychiatry at Leeds, was the chairman of a World Health Organization expert committee which has recently considered the mental health aspects of adoption. In its report (*Technical Report Series No. 70, 1953*) the committee stresses that the well-being of the child is the real aim of adoption. The family composed of father, mother, and children constitutes the normal and enduring background for a child's education, and the object of adoption is to create a relationship between adopted child and adopting parents which will resemble this as closely as possible. The child must feel certain that those around him are well disposed towards him so that without too much anxiety or sense of guilt he may be able to give expression to the complicated and often hostile feelings aroused in him by the frustrating realities of ordinary life. In former times, according to the report, the adopting family was judged merely from a standpoint of material welfare, but now there is a tendency to pay far more attention to the capacity of the adoptive family and parents to meet the child's other needs. Parents who think they could find satisfaction only in a very gifted child should be dissuaded from adopting young infants: adoptive parents must be ready to run the same risks as other parents. Other advice included in the report is that the child should be adopted at a very early age; the earlier the child knows about his adoption the better; and it is wrong to adopt a child in order to patch up an unsatisfactory marriage.

URINARY EXCRETION OF ACID PHOSPHATASE

BY

OWEN DANIEL, M.B., B.S., F.R.C.S.

PATRICIA R. N. KIND, B.Sc.

AND

E. J. KING, Ph.D., D.Sc., F.R.I.C.

(Department of Surgery and Department of Chemical Pathology, Postgraduate Medical School, London, W.12)

Marked elevation of serum acid phosphatase due to carcinoma of the prostate is often associated with evidence of impaired renal function, thus suggesting the possibility that the kidneys may excrete this substance, and that serum levels represent the balance between the rate of production and that of excretion of acid phosphatase (Daniel, 1952). It has long been known that urine is rich in acid phosphatase (Demuth, 1925), and Scott and Huggins (1942) have shown that, although most of this is added direct in the form of prostatic secretion, part is excreted by the kidneys.

The investigation reported here was undertaken with the object of discovering whether carcinoma of the prostate produced a change in the rate of urinary excretion of the prostatic (formol-stable) acid phosphatase, but the results show that there is no such change even when the serum formol-stable acid phosphatase is raised and the kidney function normal. A series of estimations was also carried out on female patients with carcinoma of the breast.

Materials and Methods

All estimations carried out were of the prostatic formol-stable acid phosphatase (Abul-Fadl and King, 1948), but for convenience' sake they will be referred to as "acid phosphatase" throughout this paper.

The total daily excretion of urinary acid phosphatase was estimated on one or more occasions on four healthy young adult males, ten patients with benign prostatic hypertrophy, seven patients with carcinoma of the prostate, nine healthy women, and 13 women with carcinoma of the breast, of whom five had bone metastases.

Males who could micturate normally were instructed to void in three parts, and the volume and acid phosphatase content of each specimen were measured separately after each micturition performed during the 24-hour test period. It was assumed that the acid phosphatase in the mid-stream specimen had been excreted by the kidneys, and that the larger amounts found in the first and last parts were derived partly from kidney excretion and partly from prostatic secretion. Patients with catheter bladder drainage passed their urine into bedside bottles, and the volume and acid phosphatase content of this were measured for 24-hour periods. It was assumed that there was no regurgitation of prostatic secretion into the bladder and that all the urinary acid phosphatase was excreted by the

TABLE I.—*Daily Excretion of Urinary Acid Phosphatase*

Name	Age	Method of Collection of Urine	Total Excretion of Urinary Acid Phosphatase (Units/24 hrs.)	Renal Excretion of Acid Phosphatase (Units/24 hrs.)	Prostatic Excretion of Acid Phosphatase (Units/24 hrs.)	Serum Acid Phosphatase (Units/100 ml.)	Renal Clearance of Acid Phosphatase (Ml. Plasma Cleared/Min.)	Renal Function	Clinical Features
A. Apparently Healthy Men (4)									
D. A. L. ..	35	In 3 parts	1,876	1,567	309	1·2	58	Normal	
			1,534	1,220	304	1·1			
			1,583	953	630	1·0	48		
W. I. S. ..	30	" " "	—	503	—	0·8	41	"	
J. A. D. ..	24	" " "	—	1,605	—	1·0	108	"	
F. R. A. ..	34	" " "	864	598	266	2·1	12·2	"	
Average:	31		1,462	1,074	377	1·2	53		
B. Patients with Benign Prostatic Hypertrophy (10)									
R. I. C. ..	72	Suprapubic catheter	—	66	—	2·0	2·3	Normal	Small fibrous prostate
M. A. R. ..	65	"	—	251	—	1·5	7·0	"	" "
T. I. S. ..	82	"	—	198	—	2·6	9·1	"	Large fibro-adenomatous prostate
D. E. N. ..	68	"	—	84	—	1·6	3·6	"	" "
D. A. C. ..	70	"	—	254	—	1·5	7·0	"	" "
S. W. A. ..	65	"	—	378	—	0·9	28·0	"	" "
M. A. D. ..	74	"	—	272	—	1·1	—	"	" "
V. E. N. ..	77	"	—	400	—	1·2	—	"	" "
P. O. L. ..	70	In 3 parts	234	212	22	2·0	—	"	" "
P. V. C. ..	72	" " "	290	222	68	0·4	8·4	"	" "
Average:	71		262	234	45	1·5	9·3	"	
C. Patients with Carcinoma of Prostate (7)									
T. E. R. ..	72	Suprapubic catheter	—	96	—	6·5	0·2	Normal	Histological diagnosis
			—	80	—	10·8	0·4	"	
			—	39	—	14·6	0·2	"	
H. O. B. ..	90	"	—	290	—	144	0·14	"	Before stilboestrol therapy
			—	360	—	144	0·17	"	
			—	41	—	40		Poor	After stilboestrol therapy
R. E. D. ..	56	"	—	254	—	2·5	7·0	"	Blood urea 60
			—	87	—	10·7		Very poor	" " 100
V. E. S. ..	76	"	—	72	—	73·0	0·06	Poor	" " 80
I. O. O. ..	73	In 3 parts	82	49	33	1·2	2·9	Normal	Clinical diagnosis
L. O. T. ..	62	"	158	158	—	2·5	—	"	Total prostatectomy for carcinoma On stilboestrol therapy
B. U. M. ..	80	Suprapubic catheter	—	12	—	2·1	0·39	Very poor	Blood urea 90
Average:				128		37·5	1·3		

kidneys.* The healthy women were instructed to measure the volume of urine passed at each micturition during the test period, and to save a part of each specimen for acid phosphatase estimation. In the case of the other women, complete 24-hour collections of urine were estimated.

Estimation of Urinary Acid Phosphatase

Twenty ml. of each sample of urine was dialysed overnight in parchment shells against cold running tap-water, the volume measured after dialysis, and any change accounted for in the final calculation. The dialysed urine was diluted, usually four times, and the enzyme content estimated by a slightly modified King–Armstrong method. 0.5 ml. of urine was added to a substrate buffer mixture consisting of 1 ml. of 0.02 M disodium phenyl phosphate, 2 ml. sodium citrate/citric acid buffer, *p*H 4.9, and 1 ml. 5% neutral formalin, and incubated at 37° C. After one hour 1.5 ml. of dilute (1 in 3) Folin and Ciocalteu reagent and 3 ml. of 15% sodium carbonate were added, and after further incubation for 15 minutes at 37° C. the colour was measured in a photoelectric colorimeter with an Ilford 608 red light filter (cf. Delory and Hetherington, 1952).

Results

Four apparently healthy males whose ages ranged from 24 to 35 years excreted in the urines a daily average of 1,462 units of acid phosphatase. Of this amount 1,074 units were calculated, on the basis of mid-stream determination, to have been excreted by the kidneys and the remaining 377 units to have been added in the form of prostatic secretion. The average serum acid phosphatase of this group was 1.2 King–Armstrong units per 100 ml., and the renal clearance of acid phosphatase, as calculated from the formula $\frac{UV}{P}$, was 53 ml. of plasma cleared of phosphatase per minute (Table I, A).

Comparison of the acid phosphatase content of the urines collected in three parts shows that the lowest values were constantly found in the mid-stream specimens (Table II),

TABLE II.—*Acid Phosphatase Content of Urine Collected in Three Parts (Units/100 ml.)*

First Part	Mid-stream Part	Final Part
149	117	720
238	134	790
260	165	630
105	91	98
127	86	127
44	25	410
9	3	13
25	14	810
99	45	770
65	32	128
41	22	620
83	38	138
Average 104	65	438

and that the last part often contained much more acid phosphatase than either the first or the mid-stream specimen. Urine was withdrawn from the bladder of three of the first group of subjects by means of urethral catheters, and the rate of renal excretion of acid phosphatase found to vary from 0.35 to 2.25 units per minute, as compared with 0.38 to 2.4 units per minute as calculated from mid-stream specimens.

Ten patients with benign prostatic hypertrophy, whose ages ranged from 65 to 85 years, excreted a daily average of 262 units of acid phosphatase from their kidneys. Two of the ten were able to collect their urines by the three-part method, and it was found that their prostates excreted an average of 45 units of acid phosphatase each day (Table I, B). The average serum acid phosphatase of the group was 1.5 units per 100 ml., and the average renal clearance of acid phosphatase 9.3 ml. per minute. Each of the ten patients had normal renal function as shown by blood urea estimations and intravenous pyelography, and in all of them the nature of the prostatic lesion was confirmed histologically.

Seven patients with carcinoma of the prostate, whose ages ranged from 56 to 90 years, excreted a daily average of 128 units of acid phosphatase from their kidneys (Table I, C). Only one of them could collect his urine by the three-part method, and it was found that his prostate excreted 33 units of acid phosphatase a day into the urethra. The average serum acid phosphatase of this group was 37.5 units per 100 ml., and the mean renal clearance of acid phosphatase 1.3 ml. per minute. The diagnosis of carcinoma of the prostate was based on histological findings in five of the patients and on firm clinical or serological grounds in the other two. Four of the patients had poor renal function as shown by raised blood urea, and their excretion of urinary acid phosphatase averaged 85 units a day as compared with 212 units a day for the three patients who had carcinoma of the prostate and normal renal function. The renal function of two of the patients deteriorated during the course of the investigation, and this deterioration was accompanied by a decrease in the excretion of urinary acid phosphatase. In one (Table I, C; R. E. D.), the serum acid phosphatase increased as the excretion of urinary acid phosphatase decreased; and in the other (Table I, C; H. O. B.) the serum acid phosphatase decreased, probably owing to the regular administration of stilboestrol.

Nine apparently healthy women, whose ages ranged from 23 to 60 years, excreted a daily average of 217 units of urinary acid phosphatase (Table III). Age, within the above limits, did not appear to have any significant effect on the rate of excretion of urinary acid phosphatase. The women with carcinoma of the breast excreted a daily average of 132 units of acid phosphatase (Table III). This was less than that excreted by healthy women. On the other hand, the women who had carcinoma of the breast and bone metastases excreted a daily average of 227 units of acid phosphatase, practically the same as in healthy women. A summary of these results is given in Table IV.

TABLE III

Initials	Age	Urine Acid Phosphatase (Units/24 hrs.)	Serum Acid Phosphatase (Units/100 ml.)	Renal Clearance of Acid Phosphatase $\frac{UV}{P}$ (ml. Plasma Cleared/Min.)
Women with Breast Carcinoma				
A. H. ..	45	93		
B. P. ..	30	85		
L. D. ..	44	102	1·4	5
D. J. ..	56	162	1·4	8·1
P. G. ..	51	118	2·7	3·0
B. L. ..	77	147	1·8	5·7
E. F. ..	48	91	1·6	4·0
N. S. ..	63	257	3·1	5·75
Average:		132	2·0	5·1
Breast Carcinoma with Secondaries in Bone				
P. T. ..	59	207	2·0	7·2
C. L. ..	53	131	2·6	3·5
M. R. ..	51	101	4·5	1·55
E. H. ..	57	230 235		
W. H. ..	54	474	1·0	33
Average:		227	2·5	11·6
Healthy Women (9)				
P. E. G.	23	205 206 208		
R. M. H.	31	260		
J. E. F. ..	30	296 292 344		
J. A. L. ..	22	127 128		
H. A. W.	32	418		
A. R. D.	23	137		
H. A. R.	60	93		
S. T. B. ..	35	165	0·5	22·5
S. T. S. ..	60	164	1·0	11·3
Average:		217	0·75	16·9

TABLE IV.—*Summary of Urine and Serum Acid Phosphatase Results*

	Total Excretion of Urinary Acid Phosphatase (Units/24 hrs.)	Renal Excretion of Acid Phosphatase (Units/24 hrs.)	Prostatic Excretion of Acid Phosphatase (Units/24 hrs.)	Serum Acid Phosphatase (Units/100 ml.)	Renal Clearance of Acid Phosphatase $\frac{UV}{P}$ (ml. Plasma Cleared/Min.)
Apparently healthy men, 24–35 yrs.	1,462	1,074	377	1·2	53
Patients with benign prostatic hypertrophy	262	234	45	1·5	9·3
Patients with carcinoma of prostate		128		37·5	1·3
4 with impaired renal function		85			
3 with normal renal function		212			
Apparently healthy women 23–60 yrs.	217	217		0·75	16·9
Women with breast carcinoma	132	132		2·0	5·1
Women with breast carcinoma and bone secondaries	227	227		2·5	11·6

Variation in the Rate of Excretion of Urinary Acid Phosphatase

During the tests on normal men and women a note was kept of the time of each micturition, and the urine of patients with catheter drainage was in many instances collected at six-hourly intervals. Information thus gained shows that the concentration of acid phosphatase excreted by the kidneys was inversely related to the rate of urine formation, and that the rate of excretion of acid phosphatase appears to be independent of the rate of formation of urine.

A slight diurnal variation in the excretion of urinary acid phosphatase was found in all subjects, but this variation did not appear to be cyclical, and in women could not be related to the menstrual cycle.

Discussion

Healthy young adults excrete a considerable amount of acid phosphatase in their urines, and of this between one-third and one-fifth can be attributed to the direct addition of prostatic secretion to the urinary stream. Comparison of the acid phosphatase content of the urines collected in three parts (Table II) suggests that the first part of micturition washes out the prostatic secretion that has accumulated in the urethra, and that straining or some other factor associated with the completion of micturition produces an immediate discharge of more prostatic secretion. The volume of prostatic secretion required to produce these effects is probably small, as the seminal plasma is rich in phosphatase—for example, that of one of the subjects contained 6,000 units of acid phosphatase per ml. The assumption that mid-stream urine is reasonably free of prostatic secretion is supported by the close correspondence between the acid phosphatase content of catheter and mid-stream specimens, although the occasional occurrence of unusually high acid phosphatase levels in mid-stream urine (Table II) can probably be attributed to the added prostatic secretion.

Men in the sixth decade and over, with benign prostatic hypertrophy, excrete approximately one-sixth the urinary acid phosphatase of younger men, and this diminution applies to both the renal and the prostatic excretion of acid phosphatase. The output of acid phosphatase in the urine of old men corresponds closely to that of women aged 20 to 60 years.

Men suffering from carcinoma of the prostate excrete slightly less urinary acid phosphatase than men of a similar age suffering from benign prostatic hypertrophy; and the difference is most pronounced when renal function is poor. There is no evidence that the excretion of urinary acid phosphatase is related in any way to serum acid phosphatase levels, and it can be concluded that the acid phosphatase put into the serum by carcinoma of the prostate is not eliminated in an active way by the kidneys.

Women suffering from carcinoma of the breast do not appear to excrete an increased amount of acid phosphatase in their urine, even though the plasma level is increased. In the cases of breast carcinoma without bone metastases the average daily excretion is lower than that in healthy women, or women with breast cancer with bone metastases.

No cause has been found for the slight diurnal variation of urinary acid phosphatase observed in all subjects or for the more marked variation in the rate of excretion that takes place throughout the day. The fact that the distribution of the rates of excretion of acid phosphatase by the kidneys of individuals fits the curve of general probability suggests that the rate is determined by many small factors operating at random and that there is no important underlying cause for the change. Calculation of the rate of renal clearance of acid phosphatase does not throw any additional light on the material studied, and merely emphasizes the inability of diseased kidneys to excrete acid phosphatase. The fact that women as well as men excreted a considerable amount of formol-stable acid phosphatase in their urine (217 units per day) shows that there must be some source of such phosphatase other than the prostate.

Summary

The rate of excretion of urinary acid phosphatase has been studied in four healthy young adult males, ten patients with benign prostatic hypertrophy, seven patients with carcinoma of the prostate, nine healthy women, and 13 women with carcinoma of the breast. Young men excrete up to six times more urinary acid phosphatase than elderly men or women of various ages. In both carcinoma of the prostate and carcinoma of the breast there was a decrease in the excretion of urinary acid phosphatase, in spite of a raised serum acid phosphatase.

This work was done in co-operation with the Institute of Urology, and we are grateful to the Institute for supplying part of the clinical material.

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The findings of a special survey undertaken after four and a half years' experience of the workings of the National Health Service are included in the annual report for 1952 of the London County Medical Officer and School Medical Officer, Dr. J. A. Scott. These include general comments on administration, co-ordination, and co-operation with other services and separate comments on the individual services. The report also includes a detailed statistical account of the "smog" catastrophe of 1952, which in the space of a week contributed to the year's total death rate an extra 0.5 per thousand population. Further statistics show that cancer is the second leading cause of death among Londoners at 2.30 per thousand and that its incidence is increasing slightly, while cardiac diseases are the first. It is reported that there is a continuing drop in the number of children under 5 years who are being immunized against diphtheria, the total percentage now being only 50. The demands on the Council's Ambulance Service were very great, as were those on the District Nursing Associations, each nurse in the service paying on an average fourteen visits a day. The report also includes a detailed account of the School Health Service. The report is published by the London County Council, and may be purchased (price 2s. 6d., by post 2s. 10d.) from the Information Bureau at County Hall, or from Staples Press, Ltd., Mandeville Place, London, W.1, or direct from any bookseller.

HISTOPLASMIN SENSITIVITY AND PULMONARY CALCIFICATION IN KENYA

BY

HUGH STOTT, M.D., D.T.M.&H.

Medical Adviser, Labour Department, Kenya

Histoplasmosis was first described by Darling (1906); Da Rocha-Lima (1912) recognized it as being due to a mycotic infection; and the causative organism, *Histoplasma capsulatum*, was first grown by De Monbreun (1934). At first the disease was regarded as a generalized and fatal illness involving the reticulo-endothelial system and often simulating visceral leishmaniasis. More recently it has been recognized that fatal cases are the exception and that there is a benign and asymptomatic form of histoplasmosis which radiologically simulates tuberculosis. There is strong evidence to show that, like tuberculosis and coccidioidomycosis, histoplasmosis will produce pulmonary calcifications observable on an *x*-ray film.

Most of the reported cases of histoplasmosis have occurred in the U.S.A., and up to 1951, 146 cases had been described, chiefly arising in the east-central area of the States. Outside the U.S.A., Mochi and Edwards (1952) were able to collect reports of 46 cases, 24 of which had occurred in South America. Only seven cases were reported from Africa, two being described from French West Africa, one from the Anglo- Egyptian Sudan, and four from the Union of South Africa.

As the result of surveys with histoplasmin-sensitivity tests, Mochi and Edwards indicated those areas, so far as have been investigated, where high, moderate, and low levels of sensitivity exist. Only five surveys have been reported from Africa, four of which were carried out in South Africa. In the Transvaal 140 persons were tested, on the Drakensberg 893, on the coast 693, and in a Durban factory 1,336 workers. The tests were performed with 1:1,000 histoplasmin, lot H 15, and the sensitivity rate ranged from 0 to 8% in the four areas. The fifth survey was carried out in Egypt, where 380 adult factory workers were tested at Mehalla with 2:1,000 histoplasmin, lot H 40. No positive reaction was observed. The criterion of a positive reaction in these surveys was an area of induration of 5 mm. or more read after 48 hours in the South African surveys and after 72 hours in Egypt.

Present Investigation

This investigation was first considered after *x*-raying some Suk tribesmen in 1949, when calcification was noted in the chest films of a few persons who showed a negative Mantoux reaction to 1 mg. of old tuberculin (O.T.) on more than one occasion. This suggested the possibility that pulmonary calcification was caused by a mycotic infection such as that due to *H. capsulatum* or to *Coccidioides immitis*. Towards the end of 1951 an opportunity presented itself for performing histoplasmin tests during the course of a survey carried out on African miners in the gold-mines and in another being carried out on prisoners in Nakuru gaol. These two groups of African males were chosen as in both cases investigations were being performed which made it necessary for tuberculin tests and a certain number of chest *x*-ray films to be done. It therefore seemed a good opportunity to carry out histoplasmin tests as an incidental investigation so that the results obtained could be correlated with the tuberculin rates and the radiological findings.

Histoplasmin Test.—A total of 833 histoplasmin tests were done—768 with lot H 42 of 1:100 dilution, and 65 with a lot obtained from the National Institute of Health, Bethesda, Maryland, U.S.A. The latter was diluted to 1:1,000. All the histoplasmin was kept in a refrigerator before use, and that of lot H 42 was all used within two weeks of dilution. The technique employed was exactly the same as that of a Mantoux test: 0.1 ml. of antigen was injected intradermally into the forearm, the result was read after 72 hours and was regarded as positive if the area of induration was 5 mm. or over at the site of injection. All areas of induration were carefully measured. The greatest care was taken to avoid using any syringes, needles, glassware, or sterilizers which had previously been used for tuberculin-testing. All the tests, both histoplasmin and tuberculin, were performed and read by me.

Tuberculin Test.—In the case of the miners both the tuberculin and the histoplasmin tests were performed at the same time, but in the case of the prisoners this was not so. All prisoners admitted to Nakuru gaol were normally tuberculin-tested on admission, and a large number of negative reactors retested routinely every three months. The same method of tuberculin-testing was used among both the miners and the prisoners. The Mantoux method was adopted, using 0.1 ml. of 1:1,000 (0.1 mg.) O.T.; it was read after 72 hours, and a positive reaction was recorded for an induration of 5 mm. or over and the presence of vesiculation was noted.

Histoplasmin Sensitivity.—Of the 768 adult African males tested with 1:100 histoplasmin, 65 (8.5%) showed a positive reaction. The average size of the reaction was 8.8 mm., the largest being 18 mm. and the smallest 5 mm. Of the 703 (91.5%) histoplasmin-negative reactors, 33 showed a minimal degree of induration after 72 hours, ranging from 2 to 4 mm., whilst the remaining 670 showed no induration whatever. Of the 65 miners tested with 1:1,000 histoplasmin, 7 (10.8%) showed a positive reaction after 72 hours; the average size of the induration in this case being 6.9 mm., the largest measuring 12 mm. and the smallest 5 mm. It will be noted that positive reactions were obtained from histoplasmin coming from two entirely separate sources.

Minimal Reactions to Histoplasmin.—An area of induration under 5 mm. after 72 hours is described here as a minimal reaction: 5.8% of the miners and 3.4% of the prisoners showed these reactions. In general a positive skin response of 5 mm. or over probably indicates specific sensitivity to *H. capsulatum*, but does not necessarily indicate the presence of active disease. Cross-reactions owing to sensitivity to other antigenically related fungi such as *C. immitis* may occur, and possibly this is particularly so among those showing small positive reactions, or negative reactors showing minimal indurations.

Histoplasmin Reactors by Tribe Groups

It was found that the reactor rate was much greater in the miners (14.6%) than in the prisoners (5.3%), although the same batch and dilution of histoplasmin was used in both groups. Almost all the miners tested were of the Jaluo or Bantu Kavirondo tribes living on or near the shores of Lake Victoria, whereas the prisoners constituted a mixed and varied number of tribes coming from widely scattered areas.

It might appear from this observation that the higher reactor rate among the miners was due to higher endemicity of histoplasmosis in the areas surrounding Lake Victoria, but an analysis of the results obtained from 110 Jaluo and Bantu Kavirondo who were tested in the prison shows that only 5 (4.5%) were positive to the histoplasmin test. It therefore seems that there is little to support the hypothesis of local endemicity, and it is possible that the higher rates in the miners may conceivably be associated with their occupation.

The vast majority of the prisoners tested came from areas in Kenya within the Rift Valley or to the west of it. It

was observed that no single tribe group in this area showed any marked tendency to higher histoplasmin-sensitivity rates than the others, but it must be pointed out that when the total numbers are divided into many groups the figures are of course small, and consequently give only a rough indication of the state of affairs.

Relationship between Histoplasmin and Tuberculin Sensitivity

In considering this relationship only the results obtained among the miners are dealt with in any detail. In many prisoners the interval between the tests varied, and to draw any conclusions from them would necessitate a difficult analysis which in the event might well prove misleading.

It was found that 91.2% of the miners were tuberculin-positive and 14.6% histoplasmin-positive. A more detailed analysis shows the following :

Tuberculin-positive,		histoplasmin-negative	..	211 (77.0%)
,,	,,	,, positive	..	39 (14.2%)
,,	negative	,, negative	..	23 (8.4%)
,,	,,	,, positive	..	1 (0.4%)

It will be observed that whereas there were 39 (15.6%) histoplasmin reactors amongst the 250 tuberculin reactors, there was only 1 (4.2%) among the 24 non-reactors to tuberculin. As cross-reactions between histoplasmin and tuberculin are extremely rare, the large proportion of histoplasmin-positive subjects in the tuberculin-positive group might be explained by presupposing contamination of the histoplasmin with tuberculin, although the greatest care was taken to avoid this complication. If such contamination had occurred, it is most probable that, predominantly, those subjects highly sensitive to tuberculin would have shown false-positive histoplasmin tests, as it is assumed that only very small traces of tuberculin would actually be injected with the histoplasmin. A response by vesiculation to the tuberculin test is indicative of a high degree of tuberculin sensitivity, and if all the vesicular reactors amongst the miners are taken it is found that out of 39 histoplasmin- and tuberculin-positive subjects only one (2.6%) showed vesiculation, whereas of 211 histoplasmin-negative but tuberculin-positive miners 10 (4.1%) showed a vesicular reaction. From this analysis it seems unlikely that contamination of histoplasmin with tuberculin resulted in false-positive reactions. The explanation for this higher percentage of histoplasmin reactors among the tuberculin reactors may be that those who had travelled to any extent were more likely to have contracted both infections than those who had remained almost exclusively in their own reserves.

The hypothesis that the positive reactions after histoplasmin were due to contamination with tuberculin becomes more unlikely when the tests performed in the prison are considered. Here, in addition to the precautions taken to prevent contamination, tuberculin tests were purposely not performed simultaneously, and yet histoplasmin reactors were still found. Furthermore, these reactions occurred in some prisoners who, either immediately before or shortly after the test, showed negative reactions to tuberculin in a strength of as great as 1 mg. of O.T.

Radiological Evidence of Calcification

There were 130 histoplasmin-tested persons whose *x*-ray films were available for examination ; 66 were miners and 64 prisoners. These *x*-ray pictures were inspected from the point of view of calcification in the lung fields or in the mediastinal glands. The interpretation and classification of calcification was based on that used by Goddard *et al.* (1949). The following standards were used :

Calcification Present.—Opacities whose size, sharpness, irregularity, and density were so characteristic that the diagnosis of calcium was indisputable. Or opacities similar to the above though somewhat less characteristic, but such that vascular structures and calcifying costal cartilages could be excluded.

Calcification Absent.—No evidence of calcification. Or opacities which possibly could be questioned as calcium but which the interpreter felt were more probably variations of the normal pattern of lung markings; particularly those shadows which might represent blood vessels on cross-section.

Each *x*-ray film was examined independently by two observers (Dr. W. S. Haynes and myself). All knowledge of the results of the histoplasmin or tuberculin tests was withheld from them. In just under 25% different results were obtained, and these films were therefore reviewed for a final assessment by both interpreters sitting together. On this occasion also the results of the histoplasmin and tuberculin sensitivity were not made available.

Selection of X-ray Films

There was to some extent a certain selection of persons whose *x*-ray pictures were examined. This was due to the fact that the films were available as a result of other entirely independent investigations which were being conducted among both the prisoners and the miners, and which necessitated taking films.

In the case of the miners a preliminary survey was being undertaken in the gold-mines of Kenya to assess the incidence of silicosis. Owing to the shortage of films it was found possible to *x*-ray only those miners who had worked for a period of five years or more underground.

The *x*-ray films of certain prisoners who were histoplasmin-tested were available because these prisoners were the subjects of a B.C.G. trial which was then in progress. For the purpose of this trial it was necessary for all prisoners who were tuberculin-negative on admission to prison, and who had a sentence of nine months or more, to have *x*-ray films taken and tuberculin tests performed every three months. Histoplasmin tests were performed on 47 of the latter subjects. Only one film from each prisoner was examined for calcification, the one selected being that taken at a date nearest to the performance of the histoplasmin test.

With regard to the relationship between radiological findings and tuberculin-testing amongst the prisoners it will be remembered that in this group the tuberculin tests were not performed at the same time as the histoplasmin tests. *X*-ray films of 47 histoplasmin-tested prisoners were available from the B.C.G. trial, and the results of the tuberculin tests performed nearest in time to the date of the histoplasmin test have been taken to indicate the tuberculin sensitivity of the individual prisoner at the time of histoplasmin-testing. In no case was the interval between the two tests more than six weeks. It should here be noted that all these 47 prisoners had at some time previously been negative to 0.1 mg. of O.T. on at least two consecutive occasions. The longest possible period between a negative tuberculin reaction and the date of histoplasmin-testing was 14 months, but a large number of prisoners had been negative reactors at a much shorter period before the histoplasmin test. All those who had converted to the Mantoux test during the interval had done so as the result either of a natural primary infection in that period or B.C.G. vaccination. It would hardly be expected, therefore, that the calcification observed in the *x*-ray films of any but those subjects longest in the trial could be due to a tuberculous infection.

Owing to an acute shortage of films it was impossible to *x*-ray all the histoplasmin reactors at the time of testing, but with the increase of supplies all the reactors who were still in prison were *x*-rayed. There were 17 such prisoners who had shown a positive or a minimal histoplasmin reaction. All of them had been found to be tuberculin-positive on admission, but had not been tuberculin-tested again, as it was presumed that they were still tuberculin-positive at the time of histoplasmin-testing. For purposes of interpretation these 17 *x*-ray films were mixed haphazardly with all the others, and could not be identified from them.

Type of Pulmonary Calcification Encountered.—Of the 130 films examined, 16 (12.3%) were deemed to show calcification. This figure should not be taken as an indication of the calcification rate existing amongst Africans as a whole, as it has already been pointed out that in the case of the prisoners there was a selection of cases. With regard to the

type and distribution of the calcification, there was evidence in 10 cases of only one area of undoubted calcification in the lung fields, and in four of an area of calcification in the lung fields with concomitant calcification at the hilum. In one case there was evidence of calcification at the hilum only; another case showed evidence of three foci in the lung fields with a calcified area at the hilum. In no case was generalized miliary calcification observed in the lung fields.

Correlation of Histoplasmin and Tuberculin Sensitivity with Radiological Findings

Correlation between calcification observed in the *x*-ray picture and the histoplasmin and tuberculin tests both of prisoners and of miners are shown in the Table. It also shows the final analysis in respect of all persons whose *x*-ray films were examined. The incidence of calcification amongst the tuberculin-positive and histoplasmin-positive group of subjects was four times that of the tuberculin-positive but histoplasmin-negative group. The same trend can be seen in the case of both miners and prisoners. If the tuberculin-negative subjects are considered the same tendency is observed—that is, a greater percentage of the histoplasmin-positive reactors show radiological evidence of calcification. This is proved by the fact that none of the 19 tuberculin-negative and histoplasmin-negative subjects showed calcification, whereas one of the three tuberculin-negative but histoplasmin-positive subjects did.

Correlation of Histoplasmin and Tuberculin Sensitivity with Pulmonary Calcification (X-ray Film)

	No. X-rayed	With Calcification		Without Calcification	
		No.	%	No.	%
Miners					
T+ H− ..	50	5	10·0	45	90·0
T+ H+ ..	11	4	(36·4)	7	(63·6)
T+ Hmin. ..	4	0	—	4	(100)
T− H− ..	1	0	—	1	(100)
Total ..	66	9	13·6	57	86·4
Prisoners					
T+ H− ..	24	1	4·2	23	95·8
T+ H+ ..	9	3	(33·3)	6	(66·7)
T+ Hmin. ..	8	1	(12·5)	7	(87·5)
T− H− ..	18	0	—	18	100
T− H+ ..	3	1	(33·3)	2	(66·7)
T− Hmin. ..	2	1	(50·0)	1	(50·0)
Total ..	64	7	10·9	57	(89·1)
Miners and Prisoners					
T+ H− ..	74	6	8·1	68	91·9
T+ H+ ..	20	7	35·0	13	65·0
T+ Hmin. ..	12	1	(8·3)	11	(91·7)
T− H− ..	19	0	—	19	100
T− H+ ..	3	1	(33·3)	2	(66·7)
T− Hmin. ..	2	1	(50·0)	1	(50·0)
Total ..	130	16	12·3	114	87·7

Hmin.=An induration of under 5 mm. occurring after 72 hours from the time of the histoplasmin test.
T+=An induration of 5 mm. or over occurring after 72 hours from the time of the tuberculin test.
H+=An induration of 5 mm. or over occurring after 72 hours from the time of the histoplasmin test.

It is of interest to note that of the 47 prisoners who were known to have been Mantoux-negative at some time within a period of 14 months of the histoplasmin test three showed calcification at the time of performance of the latter. One of these was completely negative to the histoplasmin test, and his serial *x*-ray films showed a calcification developing in a primary tuberculous lesion contracted a year before the histoplasmin test. One of the other two subjects showing calcification gave a positive histoplasmin reaction, and the other showed a minimal induration of 3 mm. to this test.

It is not possible to make a comparison of the incidence of calcification observed in prisoners and miners in view of the selection that took place among the miners.

Minimal Histoplasmin Reactions and Calcification.—The significance of a small reaction of under 5 mm. to the histoplasmin test is not known. It may indicate a past infection of histoplasmosis, or it may represent a weak cross-reaction to other fungal antigens. The Table shows that the number of persons having minimal reactions and whose *x*-ray films were available is very small, but it seems that the incidence of calcification among such people (14.2%) is not as high as among the histoplasmin-positive subjects (34.8%), and only slightly higher than that observed in those 51 unselected histoplasmin-negative miners (9.8%).

Discussion

During the past six to seven years much work has been performed with histoplasmin in various parts of the world, but there have been no recorded investigations on this subject in East Africa. The finding of an overall sensitivity rate of 8.5% among adult male Africans in Kenya suggests that histoplasmosis is endemic in at least parts of Kenya. A certain amount of caution in interpretation, however, is necessary, since it is known that weak reactions to the histoplasmin test may represent cross-reactions to other related fungi, particularly *C. immitis*. For instance, it is believed that such is the interpretation of the rather weak histoplasmin reactions observed in California, a known endemic centre of coccidioidomycosis. This explanation may be applicable to Kenya, particularly in the case of those showing small indurations, and it will be necessary to clear up this point by performing sensitivity tests with coccidioidin and histoplasmin at the same time. Induration to a greater extent than 5 mm. to the histoplasmin test may be caused after infection by other related fungi, but in the present series reactions up to 18 mm. were observed 72 hours after the histoplasmin test, and this should provide fairly sound evidence that the response obtained is specific to histoplasmin. It may, however, be that, apart from histoplasmosis, coccidioidomycosis, or indeed other similar fungal infections, is endemic in Kenya. No cases of histoplasmosis or coccidioidomycosis have yet been recorded in Kenya, but the knowledge that at any rate cases of histoplasmosis are to be expected should cause more interest in the subject and a greater search for cases.

It is difficult to explain the high sensitivity rate found among miners as compared with that of prisoners, and until further tests both with histoplasmin and with coccidioidin are performed speculation would be highly theoretical. The sensitivity rate of 14.6% found among miners is the highest rate so far recorded in Africa.

It is known that false-positive histoplasmin reactions have been caused by contamination of the histoplasmin solution or the syringes or needles with tuberculin, but it has been shown among the miners that it is very unlikely that such reactions due to tuberculin have presented as positive tests to histoplasmin. It is even more unlikely that false reactions due to tuberculin occurred when testing the prisoners, as in these subjects the chances of cross-contamination during testing were eliminated by omitting the simultaneous test with tuberculin.

The radiological appearances of healed lesions resulting from histoplasmosis usually mimic those due to healed tuberculosis (Riddell, 1951). Zwerling and Palmer (1946) stated that the appearance of massive bilateral calcification is in most instances due to histoplasmosis. In only one case in the present series was evidence of bilateral calcification found in the lung fields, and this case had a positive histoplasmin reaction. In all other cases the calcification observed was either a single focus or a dual focus similar to that seen in a healed primary complex. The picture of generalized miliary calcification which is described as occurring in histoplasmosis was not seen.

It was also found that approximately one-third of those persons reacting to histoplasmin had radiological evidence of calcification; this should be compared with about 13% of all tuberculin-positive cases that showed calcification. It

should again be emphasized in this connexion that in assessing evidence of calcification in the *x*-ray films the interpreters had no knowledge of the individual histoplasmin or tuberculin tests. These findings, although based on relatively small numbers, compare closely with those found by Goddard *et al.* among a large series of student nurses in the United States. In the latter investigation it was found that approximately one-third of the nurses reacting to histoplasmin, or to histoplasmin and tuberculin, had pulmonary calcification, whereas approximately 10% reacting only to tuberculin showed evidence of calcification.

Radiological evidence of pulmonary calcification amongst the natives of Kenya is not therefore necessarily indicative of healed tuberculosis; the evidence indicates that it may be due to a past infection of histoplasmosis. It may also be said that radiological evidence of persistent pulmonary infiltrations, as distinct from calcification, may be due to infection by *H. capsulatum*, as Furcolow *et al.* (1947) have indicated that such infiltrations in children are much more often associated with histoplasmin than with tuberculin sensitivity.

Summary

Intradermal sensitivity tests performed on 768 adult African males show an overall sensitivity rate of 8.5% to 1:100 histoplasmin. A further 4.3% of the subjects showed minimal indurations of under 5 mm. to the histoplasmin test.

It is highly unlikely that these reactions are due to contamination of the histoplasmin solution with tuberculin, but it is possible that some of the smaller reactions are due to cross-reactions with other antigenically related fungi.

X-ray films of 130 of the subjects were examined for calcification under controlled conditions. Calcification was observed in 12.3% of the films.

In the tuberculin-positive subjects the incidence of radiological evidence of calcification among histoplasmin reactors was four times the incidence observed amongst the histoplasmin non-reactors. The same tendency can be seen in the tuberculin-negative group of subjects.

Those with minimal reactions to the histoplasmin test did not show the incidence of calcification that was observed in the histoplasmin-positive group and showed only a slightly higher incidence than that of the histoplasmin-negative group.

The appearance of calcification in an *x*-ray film of a Kenya African does not necessarily indicate a past tuberculous infection, as it may be due to a past infection with *H. capsulatum*. The diagnosis of histoplasmosis should be considered in the face of a negative tuberculin test associated with a persistent pulmonary infiltration.

I thank Dr. W. S. Haynes for help in interpreting the radiographs and Professor John Crofton for reading the draft and making most helpful suggestions. I also thank Dr. R. W. Riddell for supplying the bulk of the histoplasmin, and Dr. G. C. Dockeray for the remainder. Finally, acknowledgments are due to the Director of Medical Services and the Labour Commissioner, Kenya Colony, for permission to publish this paper.

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A CASE OF PULMONARY HAMARTOMA

BY

S. D. STORE, M.D., M.R.C.P.Ed., F.C.P.S.

Lately House-Physician, Brompton Hospital, London

The term "hamartoma"—from a Greek word meaning "to err"—was coined by Albrecht (1904), who defined it as "a tumour-like malformation in which in truth one can demonstrate only an abnormal mixture of the normal developmental components of the organ in which they occur, whether it be with regard to the quantity, to the arrangement, or to the degree of development, or in all three respects." He actually used this term for cavernous malformations of the spleen and liver, and also for the fibromata of the medullary substance of the kidney. Both Goldworthy (1934) and Jaeger (1934) used the word for a similar malformation occurring in relation to bronchi. More than 125 cases have been described up to date.

The tumour varies enormously in size. Usually a globular, solid, firm growth of the diameter of a two-shilling piece, it is of greyish-white colour and has a rough nodular surface. Commonly there is round it a capsule consisting of very loose areolar tissue. Microscopically it has a characteristic picture. The predominant tissue is cartilaginous, and may show calcification or even ossification at times. Such islets of cartilage are separated by varying amounts of mesodermal and epithelial tissues, which include fibrous and adipose tissues, epithelial clefts giving at times the appearance of a gland (the epithelium may be cuboidal, columnar, or transitional), smooth muscle fibres, and blood vessels. Essentially these tumours are benign, although very rarely they may undergo malignant transformation. The case reported by Simon and Ballon (1947) did show malignant changes.

Hamartomas can occur in any part of the lung, more commonly, it is said, in the lower lobes. Most of them are peripheral and subpleural, but a few are hilar in relation to the main bronchi. They are supposed to be more common in males than in females in the ratio of 3 to 1, and can occur at any age. Jones (1949) described one in a newborn baby. However, the majority of them are seen in the middle-age groups of 35 to 50 years, perhaps because of their asymptomatic course. Clinically most of the patients are symptomless and the lesion is usually detected on routine chest radiography. When subpleural there is often pleuritic pain. When the lesion is situated at the hilum symptoms of dyspnoea due to bronchial obstruction and of cough with sputum and fever due to infection behind this obstruction may occur.

Pre-operative diagnosis is rarely possible. A rounded shadow in a chest radiograph with well-defined margins, surrounded by normal-looking lung tissue and some scattered calcium in the shadow, when seen in an asymptomatic person strongly suggest the possibility of a hamartoma. No other investigation is helpful except rarely in the hilar variety, when a bronchoscopic biopsy may prove to be diagnostic. Diagnosis is usually arrived at by thoracotomy, when the tumour alone may be removed or, if necessary, with a part of the lung as well.

Case Report

A man aged 53 first had pains in the left lower chest and upper abdomen in 1949. These were sharp and stabbing in character, and very variable in duration. Thorough investi-

gation showed nothing abnormal. In 1950 a chest radiograph showed a prominent left hilar shadow and thickened pleura at the left base. In January, 1952, these changes were well marked (Figs. 1 and 2), and he was referred to the Brompton Hospital.

In February, when first seen at Brompton, he still complained of these pains in the left lower chest and upper abdomen, and of cough with 2 to 4 oz. (57 to 85 ml.) of purulent sputum daily, loss of weight, and hoarseness of voice of about six months' duration. He was admitted under the care of Sir Geoffrey Marshall on April 7 for further investigation. On examination he was seen to be a man of average physique with a moderate degree of finger-clubbing. He had a swinging temperature rising to 101° F. (38.3° C.). A small firm lymph node was palpable above the left clavicle. On the chest a big transverse scar was seen, extending from the mid-clavicular line in the fourth left interspace across the axillary region to the inferior angle of the left scapula on the back. That was the result of drainage of an empyema at the age of 5. He also had physical signs of collapse of the left lower lobe. A provisional clinical diagnosis of bronchial carcinoma was made. The cough, with sputum and rise of temperature, was attributed to infection in the collapsed lobe.

FIG. 1.—Chest radiograph showing well-marked changes.

FIG. 2.—Lateral view.

A report by Dr. J. W. Clegg on a bronchial biopsy specimen taken on July 8 stated: "The biopsy is a small bronchial papilloma covered by epithelium showing a transitional metaplasia. Below the epithelium there are a mass of fatty tissue and a few atypical mucin-secreting glands. The appearances strongly suggest a benign hamartoma of the bronchus." A left lower lobectomy was performed by Sir Clement Price Thomas on July 18. The specimens removed at the operation showed the following features, as reported by Dr. J. W. Clegg: "Two operation specimens were received—a lower lobe and a segment of bronchus 3 cm. long dilated by an endobronchial polypoid tumour measuring 2.5 cm. in diameter. This tumour was found to consist chiefly of fat, but there were also areas of cartilage and small numbers of mucin-secreting glands present (Fig. 3). The surface of the tumour was covered by a transitional type of epithelium. These are the classical features of an endobronchial hamartoma. . . ."

FIG. 3.—Photomicrograph of specimen of tumour. (×85.)

The patient was discharged for convalescence on August 9.

Comment

When this growth occurs in the cancer age group it is almost impossible to distinguish it clinically from bronchial carcinoma, and the diagnosis is usually post-operative. This case, however, illustrates the possibility of arriving at a correct pre-operative diagnosis. Even when, as in this case, the growth is within reach of the bronchoscope it may be difficult to obtain a satisfactory bronchoscopic biopsy. The difficulty may be due to the nature of the tissues in the growth—namely, the adipose and cartilage tissues, on which the biopsy forceps slips off easily.

I am grateful to Sir Geoffrey Marshall for encouragement and most valuable guidance during the preparation of this case record, and to Dr. J. W. Clegg, pathologist to the Brompton Hospital, for the detailed report on the bronchoscopic biopsy and the operation specimens. I wish to thank Sir Clement Price Thomas for permission to report this case, Dr. J. G. Scadding for offering me the help of the Photographic Department of the Institute of the Diseases of the Chest, and Mr. D. F. Kemp for the photographs.

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EOSINOPHILS IN THE SPUTUM

BY

JOHN VAUGHN, M.D.

(From the Department of Pathology, Mount Sinai Hospital, Chicago; lately of the East African Medical Survey and Filariasis Research, Mwanza, Tanganyika)

The presence of eosinophil leucocytes in the sputum has been traditionally associated with bronchial asthma. Early writers regarded this finding as diagnostic (Bezançon and Israëls de Jong, 1912; Barth, 1921), but nowadays it has a wider significance, being found in chronic bronchitis, whooping-cough, carcinoma of the lung, etc. (Unger, 1945). The sputum eosinophilia of asthmatics was in some measure accounted for when Marchand (1915) found, in necropsies on asthmatic patients, extensive infiltration of the respiratory mucosa by eosinophil leucocytes. This is now an accepted pathological finding, as is also the infiltration by eosinophils of the nasal mucosa and sinus epithelium in other allergic states (Cooke, 1947; Baxter and Rose, 1953). Of the eosinophils in the respiratory mucosa, some were mononuclear cells, and there were many surrounding granules of an eosinophilic character; this appearance led Bezançon and Bernard (1930), Cooke (1932), and others to deduce that the eosinophils had been formed locally in response to an antigen–antibody reaction—the accepted mechanism of allergic bronchial asthma. Earlier, however, Huber and Koessler (1922) had recognized these mononuclear cells and scattered granules as stages in the degeneration of the eosinophil and had maintained the identity of the eosinophil in the lungs with the eosinophil circulating in the blood. Several attempts have been made to relate, numerically, the eosinophils in the blood with those in tissues and fluid discharges, but without much success (Cooke, 1932; Knott and Pearson, 1934; Cowie and Jimenez, 1936).

Eosinophilic infiltration of the pulmonary tissues was recently described in guinea-pigs which had developed eosinophilia following injections of toxic materials (Vaughn, 1953). In these experiments it was found that the eosinophils first increased in the circulating blood, then appeared in the lungs, and finally were found within the respiratory passages. From the chronological sequence it was suggested that the eosinophil leucocyte, formed in the bone marrow, proceeds by way of the blood stream to the lungs, migrates into the pulmonary tissues, whence it passes into the bronchioles and bronchi, and so is discharged from the body.

While working among the natives of Sukumaland, in Tanganyika, it was noticed that many specimens of sputum contained eosinophil leucocytes. The relationship which this finding might bear to the high incidence in the local population of parasitic disease, and, of course, to the eosinophilia of the blood so often an accompaniment to it, was considered and an attempt made to assess this relationship. Consequently the simultaneous examination of blood and sputa from a group of the local African natives was undertaken.

Methods and Results

African natives attending the out-patient department of Mwanza Hospital comprised the test group. These patients were not selected in any way except that in view of the difficulty of obtaining specimens of sputum from young children such cases were omitted. There were only 10 cases of clinically apparent respiratory disorder in the whole series.

Patients were invited to expectorate into a Petri dish and smears were made of suitable specimens. Those specimens which consisted only of saliva were rejected and the patient was encouraged to try again. The smears were fixed, while still wet, in Schaudinn's fluid and were subsequently stained by haematoxylin and eosin, two such smears from each patient being examined. Differential leucocyte counts were found to be unsatisfactory owing to the uneven, often focal, distribution of the eosinophils. It was felt that a general impression of the contents of the smears as a whole would be of more value, and thus the smears have been reported as containing no eosinophils, scanty eosinophils, small numbers, or moderate to large numbers of eosinophils. Eosinophil counts of the peripheral blood were carried out by the method of Thorn *et al.* (1948).

In all, 205 Africans were examined in this way, and by a simple coding procedure examinations of the blood and sputum were made in complete independence.

In the Table the frequency and density of eosinophils in the sputum are shown in the various groups of Africans examined, the patients being arranged according to the level of eosinophils in the peripheral blood.

Occurrence and Intensity of Sputum Eosinophilia in 205 Africans with Various Levels of Eosinophil Leucocytes in the Peripheral Blood

Eosinophils in Sputum	Eosinophils in Peripheral Blood		
	0–500/c.mm.	501–1,000/c.mm.	Over 1,000/c.mm.
None	40	14	6
Scanty	18	21	3
Small No.	12	28	26
Moderate to large No.	3	12	22
No. of patients ..	73	75	57

Discussion

Of the patients examined, nearly two-thirds had an eosinophilia of 500 or more eosinophil leucocytes per c.mm. of blood, and the general pattern seems to be that as the degree of eosinophilia increases so does the frequency and density of the eosinophilia of the sputum. About one-fourth of the cases, however, do not follow this trend, some eosinophilic patients showing no sputum eosinophilia and some non-eosinophilic patients having numerous eosinophils in the sputum. To assess the importance of these dissenting results, attention must first be drawn to the technical inaccuracies in estimating the frequency of eosinophils in the smears. Also, in the animal experiments quoted above, eosinophilia of the blood was not synchronous with the appearance of these cells in the bronchioles, there being a time lag of some hours. This time lag was also evident as the eosinophilia subsided. This asynchronism has been observed in asthmatics. Tuft (1949) remarks that eosinophils in the sputum "are especially abundant towards the end of the attack." Generally, however, the trend of the present findings does support the view that eosinophils appear in the sputum, and of course in the tissues of the lungs, as late stages in the course of an eosinophilia.

The failure of former workers to establish such a correlation probably lies in their having investigated cases of allergy, the antigenic stimulus of which may not have been enough to produce an eosinophilia of sufficient intensity or duration to permit the relationship to be observed. In the present study the eosinophilia in almost all cases was a response to parasitic infestation, and it is among such cases that some of the highest eosinophil counts have been encountered (Wintrobe, 1951). In one of the cases included here there was a peak eosinophil count of 18,800 cells per c.mm., and the eosinophilia persisted for 10 days.

In a highly parasitized community such as that here examined, the frequency of eosinophilia, including pulmonary eosinophilia as revealed by the sputum, is not a new finding, for there have been many reports associating eosinophilic infiltration of the lungs with parasitic disease (Söderling, 1939; Wintrobe, 1951). The infiltration syndrome (Loeffler, 1932) should thus be expected in any condition in which there is a substantial increase in the number of circulating eosinophil leucocytes for any length of time—for example, periarteritis nodosa (Middleton and Carter, cited by Tisell, 1941).

As evidence accumulates there seems to be less doubt that the state of eosinophilia, of whatever primary aetiology, embodies an increase in the number of eosinophil leucocytes circulating in the blood, their subsequent migration (? selective segregation) into the tissues of the lungs, and their eventual discharge into the respiratory passages and so out of the body.

Summary

Simultaneous examination of blood and sputum for eosinophils was made in 205 African natives in an area where the incidence of parasitic infestation is high.

The results obtained suggest that there is some association between eosinophilia of the blood and that of the sputum.

This association is discussed in relation to the reports of pulmonary eosinophilic infiltration complicating parasitic disease.

It is suggested that eosinophilia of the sputum and its preceding eosinophilic infiltration of the lungs are integral parts of a general eosinophilia, and that the demonstration of eosinophils in sputum indicates that an eosinophilia is or has recently been in progress.

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The annual report of the National Institute for the Blind draws attention to the manifold activities now being undertaken by that organization. Of particular interest is the development of the new solid-dot Braille, which composes dots of plastic ink on paper instead of impressing them, and which will make possible the much cheaper production of books, periodicals, music, etc., for the blind. Moon type is a useful complement to Braille, especially for those who become blind in old age. It was developed by Dr. William Moon (1818–94), who lost the sight of one eye at the age of 4, following an attack of scarlet fever, and became totally blind at the age of 22. Although Moon literature is costly to produce, the Institute has continued to supply it. Nearly 50,000 volumes of literature and 2,000 volumes of music were among the year's output of the Institute during the year. The physiotherapy school continues to make its useful contribution to medicine; an arrangement made with the Whittington Hospital, Highgate, has enabled skilled physiotherapy students of the Institute to give 4,000 treatments a month to out-patients. The Institute has begun a new policy whereby its members may obtain Braille watches, clocks, literature, and other goods at greatly reduced cost.

Medical Memoranda

Prevention of Post-operative Backache in Women

Some women suffer from low backache following prolonged abdominal or vaginal operations. The pains are sometimes so excruciating after awakening from the anaesthetic (and commonly during the first post-operative day) that only morphine brings relief. Some of these patients say that they suffered more from the backache than from the effects of actual operation, and this backache may persist for months after the operation.

This kind of backache is due to the forcible flattening of the lumbar spine curvature while the deeply anaesthetized patient is stretched out on a flat operating table. During vaginal operations in the extreme lithotomy position this flattening of the curvature is aggravated by extreme flexion of the thighs. The pains are caused partly by pulling on the interlumbar and sacro-lumbar ligaments, which sometimes leads to slight dislocation of the intervertebral joints.

In other patients, predisposed to degenerative changes in the intervertebral disks, the widening of the lumbar bodies by the forcible flattening of the curvature leads to some protrusion of a disk or disks, with resultant pressure on the dura mater, causing pains similar to those of the common disk lesions. Cyriax calls this kind of pain "dural pains." Deep anaesthesia leads to relaxing of the lumbar muscles, which facilitates the flattening of the curvature. Since the introduction of the relaxing curare preparations the evidence tends to suggest that this kind of backache has become commoner.

In women operated on in the lithotomy position another factor may add to this flattening of the lumbar curvature. If, after the operation, the legs are not put gently into the normal position, but instead one leg is first stretched while the other is still fixed to the stirrup, undue force is applied to the sacro-iliac joints, causing strain to the ligaments and resulting in mild dislocation of these joints.

The flattening is still further increased by the routine nursing with pillows arranged in such a way that the lumbar region remains unsupported. Nurses have for years been trained to adjust the pillows in this manner; four to six pillows are usually placed under the shoulders and back to keep the patient in a propped-up position, but no attention is paid to the fact that the lumbar region is left entirely unsupported. One can push a hand underneath, as if in a tunnel. Consequently the already flattened curvature resulting from lying on the operating table is still unsupported, and so the back pains are increased.

A fourth contributory factor is a mattress which is too soft in texture; this gives too easily, causing dents and so contributes to the flattening.

Two types of women are prone to such post-operative backache—the very stout and the asthenic flabby type. In the former the lumbar muscles are permanently strained in balancing the heavy abdominal weight. These women always have an increase of the lumbar curvature, and during the operation the already overtired lumbar muscles readily give way. The second type have muscles and ligaments constitutionally weak. The intervertebral ligaments are very loose and the spine curvature relaxes easily.

These unpleasant backaches can be prevented by a very simple procedure: (1) During the operation a cushion, not too soft, should always be placed under the lumbar curvature to prevent flattening of that part of the spine. (2) When the patient is changed from the lithotomy to the normal position both legs should be stretched gently at the same time. (3) Nurses should be taught never to allow the lumbar region to be unsupported while the patient is lying on her back, and especially during the first few days after the operation. An ordinary and not too soft pillow

should always support the lumbar region and should be rearranged several times during the day; and the mattress should not be too soft.

Should backache occur in spite of these precautions, a tight strapping of the lumbo-sacral region usually gives relief in a short time.

It is extraordinary, however, how difficult it has proved to get these simple precautionary measures introduced and carried out by nursing staff. Doubtless this is due to the rigid routine instruction during training; and to get nurses to alter this routine may prove extremely difficult, as I have found. Nevertheless when they have put these measures into practice great suffering has been spared to these patients and their convalescence has been made much easier and swifter.

E. SCHLEYER-SAUNDERS, M.D., F.I.C.S.

Investigations on Long-acting Corticotrophin

Corticotrophin remains in the body for only a short time after administration. Sayers *et al.* (1949) found, in two normal persons, the highest blood concentration at the conclusion of intravenous infusions for a half and one hour respectively, whereas three hours after starting the infusions the corticotrophin level had fallen to the control value.

While the decrease in number of eosinophil leucocytes is accepted as a standard for increased activity of the adrenal glands, it is known that the number of eosinophil leucocytes in the blood does not decrease after a single intravenous injection of corticotrophin (Renold *et al.*, 1952). One intramuscular injection daily, given on three consecutive days, does not stimulate the adrenal cortex as measured by the excretion of 17-ketosteroids in the urine (Querido *et al.*, 1951). The daily therapeutic dose of corticotrophin must therefore be subdivided. This is inconvenient for the patient as well as for the nursing personnel, and consequently a search has been made for an A.C.T.H. preparation which will be effective when injected only once daily. The preparations described below seem to meet these requirements.

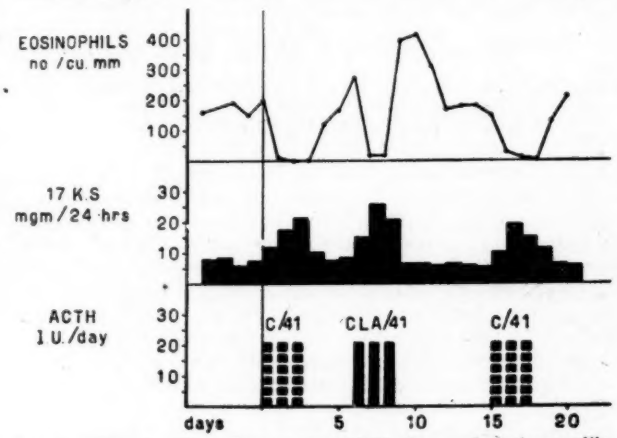

FIG. 1.—Case 1. The effect of six 3½-I.U. doses of corticotrophin a day compared with that of one dose of 21 I.U. of long-acting corticotrophin of the same batch.

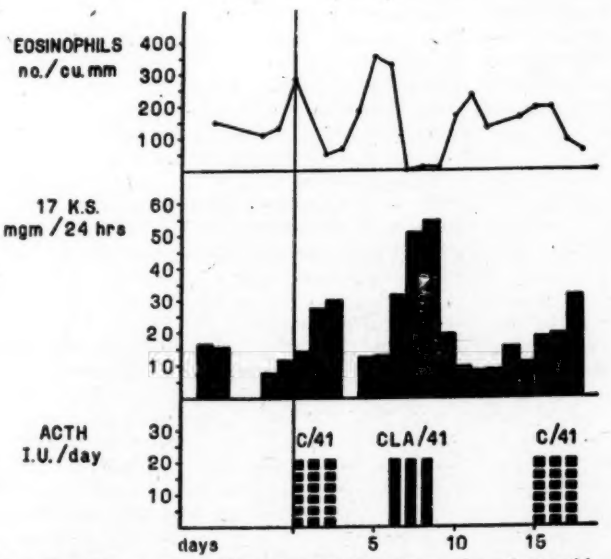

FIG. 2.—Case 2. The effect of six 3½-I.U. doses of corticotrophin a day compared with that of one dose of 21 I.U. of long-acting corticotrophin of the same batch.

Methods.—Using the method described by Goslings *et al.* (1953), we gave six 3½-I.U. doses of the Organon preparation C/41 daily to two male patients suffering from rheumatoid arthritis. The results were compared with those from one 21-I.U. dose of the Organon long-acting (CLA) preparation of the same batch. In the intervals the patients were given dummy injections. The 17-ketosteroids excreted in the urine in 24 hours were assayed according to the method of Kassenaar *et al.* (1950). Eosinophil leucocyte readings were taken every morning at the same time, before breakfast and previous to the first injection, and the cells were stained according to the method of Zollikofer (1901).

Results.—The eosinophil leucocytes showed a distinct decrease during injection of the normal preparation (C), and also during that of the long-acting preparation (CLA) (Figs. 1 and 2). Both C and CLA had a marked effect on the excretion of 17-ketosteroids in the 24-hour urine. In Case 1 (Fig. 1) these values were of the same order of magnitude; in Case 2 (Fig. 2) the excretion was about 80% more during the CLA-period than during the period in which the normal preparation was given.

DISCUSSION

From the criteria of Goslings *et al.* (1953) it may be concluded that CLA has a satisfactory action. This is in accordance with the clinical results obtained by us, and by others (Solem and Holterman, 1952) with zinc-protamine preparations. It is not intended to discuss the validity or otherwise of the Sayers test for corticotrophic preparations. It is important, however, to remember that this test requires intravenous injections, and that only the immediate effect is measured. The long-acting preparations do not lend themselves to intravenous injection, and their effect is spread out over a longer period. It does not seem correct, therefore, to express the strength of a CLA preparation in Sayers units of the basic material from which these preparations are made. Furthermore, it is possible that in preparing CLA some change in the activity occurs.

In order to obtain reliable data on long-acting preparations for clinical use it seems necessary to compare these preparations with ordinary preparations of the same batch, based on the excretion of 17-ketosteroids in the urine in men.

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A. A. PIT,
Research Fellow in Medicine,
"Stichting Leidse Rheumatologische Kliniek."
A. CATS,
Research Fellow in Medicine,
National Health Council.
A. A. H. KASSENAAR, Ph.D.,
University Hospital, Leyden, Holland.

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Reviews

ANOXIA OF THE NEWBORN

Anoxia of the New-Born Infant. Consulting Editors: Dr. K. W. Cross (U.K.), Dr. M. Lelong (France), Dr. C. A. Smith (U.S.A.). Editors for the Council: J. F. Delafreshaye and T. E. Oppe. A Symposium organized by the Council for International Organizations of Medical Sciences. (Pp. 230; illustrated. 27s. 6d.) Oxford: Blackwell Scientific Publications. 1953.

When 17 outstanding authorities combine to discuss their subject informally among themselves their confabulations should make informative reading. This monograph is certainly informative; it is also stimulating and provocative. When obstetricians and paediatricians agree about the care of the newborn, and when, joined by pathologists, anatomists, physiologists, and chemists, they can meet together daily for five days "in a tranquil setting," then indeed are the lions lying down with the lambs.

Anoxia, a term which has now superseded the old "white" and "blue asphyxia"—and very properly so—is the subject of many theories but, in its essentials—prevention, early diagnosis, and treatment—of but few facts. In this symposium the theories are discussed and many are discredited, a number of new facts are brought forward, and alternative theories are proposed in the light of the authors' own research. Such vexed questions as the aetiology of hyaline membrane, the significance of foetal haemoglobin, and the value of combining carbon dioxide with oxygen in treating anoxia are fully considered. Dr. Lind (Stockholm) presents results of angiocardiographic studies on foetuses and newborn infants, offers an explanation of the effect of anoxia on the functional closure of various foetal blood channels, and confirms the value of gastro-intestinal oxygen therapy.

There are five main sections which follow an introduction by Dr. Lelong (Paris). Each section ends with an account of the discussion engendered by the papers. The first is devoted to clinical aspects, with particular reference to the early diagnosis of foetal anoxia (Dr. Mayer, Paris), the mechanism, prevention, and treatment of anoxia (Dr. Gibberd), and the treatment of respiratory difficulties in premature infants (Dr. Rossier, Paris); the second to pathological findings—a symposium by Dr. Lelong, Dr. Clement Smith, Dr. Agnes Macgregor, and Dr. Ahvenainen (Helsinki); the third and fourth to biological and physiopathological considerations respectively; and the fifth to the place of oxygen in the therapy of premature infants and the treatment of atelectasis. In the final section some of the general conclusions are worthy of note, particularly in relation to anaerobic metabolism, arterial oxygen saturation, and oxygen therapy. It is stressed that the aim of resuscitation in anoxia is to oxygenate the medulla rather than to try to cause total expansion of the lung. Any mechanical device for resuscitation should be safe, simple, and readily applied without complicated apparatus or special skill.

Here indeed is a mental feast for all paediatricians, a book of value to all research workers in the field of neonatal physiology and pathology. It is well produced, with an extensive bibliography and excellent photomicrographs, graphs, and angiographs.

WILFRID GAISFORD.

PNEUMOCONIOSIS ABSTRACTS

Pneumoconiosis Abstracts. Volume I. Reprinted from the *Bulletin of Hygiene*, 1926–1938. (Pp. 347; illustrated. 63s.) London: Sir Isaac Pitman and Sons. 1953.

This book is the first of two volumes in which will be collected all the abstracts relating to pneumoconiosis which were published in the *Bulletin of Hygiene* from 1926 until the end of 1950. The present volume contains those abstracts published from 1926 to 1938. Dr. E. L. Middleton, who has been responsible for the selection of relevant abstracts and for the preparation of the index, has adopted a broad definition of pneumoconiosis to cover all forms of pulmonary reaction to inhaled dust, without any reference to effect on function, and has taken the word "dust" to include fume in the solid state. The abstracts therefore cover a wide field of interest. They are grouped in sections, whose headings indicate their scope. After a general section on industrial hygiene and the relation of occupational dusts to respiratory disease in general, there are sections on silicosis, asbestosis, pneumoconiosis of coal workers, pneumoconiosis caused by other inorganic dusts and by dusts of vegetable origin, and on respiratory disease caused by fumes. These are followed by a section on methods of dust suppression and of protection of the worker against dust. The next two sections are on the periodical reports of various official bodies relating to pneumoconiosis and on pneumoconiosis legislation. Finally, there are a number of book reviews.

The value of such a compilation depends in great measure upon the accuracy and completeness of the index. In this volume the index covers 21 pages in double column, and has obviously been prepared with scrupulous care; a few random tests of it have proved entirely satisfactory. This volume, together with its companion, is likely to prove indispensable to everyone interested in the problems of industrial pulmonary disease.

J. G. SCADDING.

MEDICAL EDUCATION IN THE U.S.A.

Medical Schools in the United States at Mid-Century. By John E. Deitrick, M.D., and Robert C. Berson, M.D. (Pp. 380; £1 16s.) London: McGraw-Hill Book Company. 1953.

Medical schools are an expression of the life of a nation, and therefore reflect its social, economic, and political forces; but the response of medical schools to changes in these forces is not instantaneous, and periods of confusion and stocktaking precede readjustment. In the United States medical schools have been evolving continuously for the past two centuries, the tempo varying with events, and there is no sign of finality. That the second world war has created immense problems is evident from this book, which will take its place in the series of classic reports initiated by Abraham Flexner in 1910.

The authors worked for the "Survey of Medical Education," whose committee includes some of America's leading medical educationists. The book is wider in scope than its title suggests, being in fact a comprehensive review of medical education, both undergraduate and postgraduate; the schools themselves are simply the focal point. As Alan Valentine says in his foreword, the book is the first thorough self-evaluation of American medical schools for many years. The materials were collected by questionaries and visits to a large and representative proportion of the schools, with the full co-operation of deans, staff, and students. The result is much more readable than might have been expected. The book is concise, well-written, and trenchant, each section having a good summary and a list of recommendations appended; and the occasional platitudes may well bring home important truths to some readers for the first time.

The functions of a medical school are distinguished as education, research, and "service." Finance and administration are discussed at length, the topics including the cost of educating a medical student, the relation between medical school and hospital, the organization of departments in medical schools, medical libraries, teaching staff, and the selection of students. The rest of the book is on the theory and practice of the education of students and doctors, and there are interesting appendices, especially one on what students think.

While many of the problems discussed are peculiar to the United States, arising from a political and financial situation very different from ours, some are met with

everywhere. Among those of interest to us are the problems of medical libraries, the overloaded curriculum, encroachment on the student's leisure and vacations, out-patient teaching, domiciliary teaching, and the functions of housemen. British medical teachers and deans would find this record of American experience directly relevant to their own problems. If any British students read it, they will learn that talking to the blackboard and mumbling into one's beard are not peculiar to British teachers, and that British and American students are alike in desiring closer association with the staff.

RAYMOND WHITEHEAD.

PRACTICAL PRESCRIBING

Practical Prescribing: An Introductory Guide for Medical Students. By Alastair G. Macgregor, M.D., B.Sc., M.R.C.P.(Lond.), F.R.F.P.S., and Trevor W. G. Kinnear, M.B.E., M.B., Ch.B., M.R.C.P.(Ed.), M.R.C.P.(Lond.). Foreword by Professor J. H. Gaddum, F.R.S. (Pp. 88. 6s.) Edinburgh and London: E. and S. Livingstone. 1953.

This manual is an introductory guide for medical students. The authors therefore give the bare essentials about dosage, prescription writing, prescribing within the terms of the National Health Service, the law and drugs, and methods of administration of drugs. They make no attempt to present prescribing as an art. Further, we are told that "Signetur" in the form of "Sig." is the only permissible Latin word to appear on a prescription, just as ℞ is the only permissible symbol. We have as an example of a typical prescription "℞ Ferrous sulphate tablets (B.P.)" with the usual directions in English. So be it! We must move with the times even though we may sigh nostalgically for our basis, adjuvant, corrective, and excipient compounded with a fine knowledge of incompatibility and rendered more efficacious by indecipherable dog Latin. There are surely two strong reasons against the jettisoning of Latin: first, speed is gained by using truncated Latin terms; secondly, such a prescription can be understood and thus dispensed over the greater part of the globe.

On page 37 we read that "the danger of diamorphine addiction is so great that this otherwise useful drug has been omitted from the latest edition of the B.P., 1953." This regrettable and ridiculous action might well have been accorded a paragraph of criticism, otherwise the student may conclude that it meets with general approbation. On the same page it is stated that Indian hemp has no legitimate medicinal use, yet as a euphoriant it is the only drug extensively used in the treatment of the anxious patient with duodenal ulcer.

The authors have presented their subject with praiseworthy clarity.

A. H. DOUTHWAITE.

PSYCHO-ANALYTIC PAPERS

Primary Love and Psycho-Analytic Technique. By Michael Balint, M.D., Ph.D., M.Sc., L.R.C.P., L.R.C.S. International Psycho-Analytical Library. No. 44. (Pp. 288. £1 10s.) London: The Hogarth Press, 1952.

Dr. Balint, one of the most distinguished of Ferenczi's pupils in this country, has taken after his master in three main respects—his interest in psychological parallels to the laws of biogenetics, his theoretical and practical concern with the development of libido-theory, and his tendency to speculative handling of psycho-analytical problems, in particular the rationale of psycho-analytical therapy. The present volume consists of papers delivered between 1930 and 1952 and includes discussion of such subjects as pregenital organizations, primary love, genital love, love and hate, transference and counter-transference, therapeutic aims and techniques, and the termination of analysis. These subjects the author deals with in an easy speculative manner, the effect of which naturally depends on the degree to which the reader is ready to accept the interpretations so disarmingly presented.

On the matter of biological parallels it cannot be forgotten, however, that psychologists can quote biological and anthropological scripture for their own purposes. And when one examines closely the clinical observations on which Dr. Balint's theories are founded one is occasionally disconcerted to find such statements as "coitus . . . begins as an altruistic act," which is either an instinctual truism, a verbal misunderstanding, or a clinical understatement. Even his technical aphorisms are sometimes naive—as where he says that *a priori* there is no reason why patients should not be able to produce their symptoms at will after treatment "now that they have become fully conscious of their individual mechanisms of production." Similarly his favourite thesis that in a satisfactorily terminated analysis the patient makes a "new beginning" free from anxiety is either a restatement of the obvious or a professional idealization of the analytical process.

Dr. Balint's most important service is the emphasis he lays on early loving object-relations. Whether or not one agrees with his concept of "primary love" (primitive archaic object-relation), he is undoubtedly correct in his criticisms of some modern tendencies of psycho-analysis whereby constitutional sadistic and masochistic tendencies are unduly stressed.

EDWARD GLOVER.

TEN TEACHERS

Diseases of Women. By Ten Teachers, under the direction of F. W. Roques, M.D., M.Chir., F.R.C.S., F.R.C.O.G. Ninth edition. (Pp. 480; illustrated. 28s.) London: Edward Arnold and Co. 1953.

The production of the new edition of this well-known 34-years-old textbook is under the direction of F. W. Roques, assisted by J. Beattie and J. Wrigley as co-editors. Nearly all the London teaching schools are represented in the list of contributors, which now includes S. Clayton, C. Gwillim, and T. Lewis in the places of F. Cook, Sir William Gilliatt, and C. White. The principle of collective responsibility, which has the doubtful merits of eliminating heresy and ensuring that nothing is said which would not bear repetition before the most narrow-minded examiner, has the known disadvantage of resulting in an insipid milk-and-water concoction which hardly dares to express a definite opinion. This disadvantage is now recognized, and a serious attempt has been made to allow each contributor sufficient rope to give the book more courage and character, and to inspire the reader with more confidence. The attempt is by no means unsuccessful. Moreover, attention is paid to the changing outlook on the requirements of the undergraduate in that the section on operative treatment is shortened and simplified, while more emphasis is placed on medical gynaecology. The chapter on neurasthenia and neurosis in relation to pelvic disorders deserves special mention. The illustrations are reasonable in number and generally adequate though individually varying in quality.

The student may wish for more on some of the common practical problems such as vaginal discharges and pruritus vulvae, but it is difficult to see how it could be supplied without increasing the size and price of the book—which would be a pity. As it is, the editors and contributors are to be congratulated on the way in which they have moulded advances in knowledge and modern trends in thought around the age-old essentials of gynaecology, and have still managed to keep it within small compass. For this as well as for other reasons it will undoubtedly find favour among large numbers of present-day students, as did its predecessors with previous generations.

T. N. A. JEFFCOATE.

Therapie der Kinderkrankheiten by Professor J. Siegl (Vienna: Wilhelm Maudrich, 1953. M. 32) is a product of the Vienna school of paediatrics and is volume five of a series on paediatric subjects. After an account of feeding normal infants, it goes on to discuss the treatment of diseases of the newborn, and then other disorders of childhood. An appendix lists certain drugs and prescriptions, and discusses dosage.

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CORTISONE AND BLOOD DISEASES

During the last three years A.C.T.H. and cortisone have been increasingly used in the treatment of blood diseases. Since quite large numbers of patients have now been treated,[1-3] it should be possible to form some sort of judgment on the value of these drugs. Only in acquired haemolytic anaemia of the auto-antibody type and in idiopathic thrombocytopenic purpura have favourable responses been obtained with any regularity. In other types of haemolytic anaemia, in agranulocytosis, chronic leukaemia, myelosclerosis, reticuloses, and in aplastic anaemia the drugs have given far less benefit, a favourable response being a rare and unpredictable event. The acute leukaemias occupy an intermediate position, for some cases in childhood will respond, even dramatically.

Before the physician undertakes the treatment of blood diseases with these drugs he should have gained experience of their general metabolic effects, for they may have to be given for long periods in large doses —for example, in adults up to 300 mg. a day of cortisone or 200 mg. a day of A.C.T.H. or its equivalent as A.C.T.H. gel in divided intramuscular doses. Most patients with acquired haemolytic anaemia of the auto-antibody type, whether "idiopathic" or secondary to some other disorder, respond favourably to treatment; some may obtain complete clinical and haematological remission. A.C.T.H. or cortisone therapy should therefore be the treatment of choice for acquired haemolytic anaemia, and splenectomy, which results in clinical cure in not more than 50% of cases,[4] should be kept in reserve. If a patient responds to hormone therapy, it seems reasonable to reduce the dosage to the minimum amount that will prevent his haemoglobin level from falling below 11 g. per 100 ml. (74%). It is doubtful if it is worth trying to obtain normal haemoglobin levels by increasing the dosage to perhaps dangerous levels, for there is no evidence that A.C.T.H. or cortisone can cure the patient's disease. The aim should be to control the rate of haemolysis in the hope that spontaneous cure will take place. In some cases treatment may have to be prolonged. In our opening pages this week Drs. G. M. Aber and G. N. Chandler and Professor S. J. Hartfall describe the follow-up of a child whose earlier history had been reported by Rose and Nabarro[5]; this patient (who had undergone splenectomy) still needed 75 mg. of cortisone a day 60 weeks after the beginning of therapy for the control of haemolysis.

The place of splenectomy in the treatment of acquired haemolytic anaemia needs to be reconsidered in the light of the favourable results of hormone therapy. Unfortunately there does not seem to be any way of telling beforehand which patients will do well after the operation; in particular, a favourable response to A.C.T.H. or cortisone does not necessarily mean that splenectomy will be successful, nor is the converse true. It is probably wise to postpone splenectomy either until it is clear that the patient will not respond to A.C.T.H. or cortisone in large doses and that his illness shows no signs of abating, or until it is clear that large doses of the hormones are required to control the patient's anaemia and that after months of treatment there are still no signs of a remission. In the latter circumstances, even if clinical cure does not result from operation, it may be possible to keep the patient well on smaller doses of A.C.T.H. and cortisone than previously.

As to idiopathic thrombocytopenic purpura, the situation is analogous to that of acquired haemolytic anaemia; most of the patients are benefited by hormone therapy whether the platelet counts rise or not. In acute cases cortisone or A.C.T.H. should be the treatment of choice, but when the disease is running a chronic course splenectomy will probably have to be undertaken sooner or later. The place of A.C.T.H. and cortisone in the treatment of acute leukaemia is more controversial. It seems that a favourable response may be expected only in acute or subacute lymphatic leukaemia affecting children or adolescents. In adults the chances of a remission are remote, and in children acute and subacute myeloid forms usually fail to react. According to Dameshek[6] the best results are obtained if A.C.T.H. and small doses of aminopterin are given together. Unfortunately, even if remissions occur, they are always temporary, relapse inevitably taking place sooner or later. Most commonly the remissions last a few weeks; they seldom last more than four months. This raises the question whether treatment is worth while; on this crucial point opinions naturally differ. The simplest solution is to give children and adolescents suffering from acute leukaemia the benefit of A.C.T.H. or cortisone treatment. Unlike

[1] Dameshek, W., *British Medical Journal*, 1952, **2**, 612.
[2] Medical Research Council Haematology Panel's First Report, ibid., 1952, **1**, 1261.
[3] Medical Research Council Haematology Panel's Second Report, ibid., 1953, **2**, 1400.
[4] Welch, C. S., and Dameshek, W., *New Engl. J. Med.*, 1950, **242**, 601.
[5] Rose, B. S., and Nabarro, S. N., *Arch. Dis. Childh.*, 1953, **28**, 87.
[6] *British Medical Journal*, 1953, **2**, 825.
[7] Dacie, J. V., *et al.*, ibid., 1950, **1**, 1447.

treatment with anti-folic-acid drugs[1] the consequences of overdosage are not serious and distressing; and, if remission follows, the parents of the patient may find that the respite has given them time to adjust themselves to a tragic situation.

TOO MANY DOCTORS?

The beginning of a new year is apt to prompt speculation on the future, and some thought is needed on what should be done about the ever-growing numbers of the medical profession in Britain. Against the hosts of applicants besieging their deans, the medical schools erect some sort of a barrier, with the result that during the last six years the annual entry of students to the medical schools of the United Kingdom and Eire has been between 2,500 and 2,700. The effect of this on the *Medical Register*, after some names have been removed by death and other causes and a few others added, has been to increase the total of registered medical practitioners by about 1,000 a year over the same period. Doctors seeking permanent positions are finding it more difficult than formerly to get the jobs they want, and the deans of the medical schools have a responsibility in relating supply to demand which they are at present compelled to exercise without sufficient knowledge of the country's needs. While the *Register* is likely to show at least the present rate of annual increase for the next five or six years, by virtue of the numbers of students now in training, the question whether these increments should be allowed to continue, and for how long, is surely an urgent one.

A fair approximation to the number of medical practitioners of all kinds in England and Wales and in Scotland may be obtained from the *Medical Directory*. This shows that in 1953 there was in England and Wales one doctor to every 900 persons and in Scotland one to every 600. These figures are of residents in the countries concerned, and do not attribute to Scotland those many doctors who qualify there but practise elsewhere. Some doctors whose names appear in the *Directory* have retired, and some whose names are not listed in it are yet in practice; the difference between these two numbers is unknown, but it is unlikely to be a large source of error in the final figures. In 1939, according to the same source, there were 37,429 doctors in England and Wales, while in 1952 there were 50,574. This is an increase of about 13,000, or 35%. In Scotland, the numbers rose over the same years from 6,091 to 9,096, an increase of about 3,000, or 50%. The *Medical Register* tells much the same tale: between 1939 and 1952 the numbers for England, Wales, and Scotland rose from 63,360 to 83,914, an increase of about 20,000, or 33%. If this expansion continues, it will soon be impossible for some medical men to find work in Britain, and the scope for practice abroad is now much less than it was.

A year ago the Council of the B.M.A. accepted a suggestion made by the chairman of the General Medical Services Committee that the Committee should look into this question of supply and demand. A subcommittee was appointed, and it reported to the G.M.S. Committee on December 17.[1] Acknowledging that the task is complex and that national policy must be determined by the country's need for medical men and women, the G.M.S. Committee is recommending the B.M.A. Council to invite the Ministry of Health to co-operate in the setting up of a working party. The task of this new committee would be "to examine on a long-term basis and with the widest possible terms of reference the future number of medical practitioners likely to be required in all branches of the profession and to relate these needs to the intake of students to the teaching schools."

Some much-needed information could be gathered from such an inquiry, though there are two hazards to be avoided. The first is too great a preoccupation with details. Any attempt to lay down precisely how many doctors should fill any particular branch of the profession must be put out of court, for it is impossible to impose on the whole of medicine the sort of staff establishment that suits Government services. The expansion of medical knowledge in the past two or three decades has been reflected in a greatly altered distribution of medical men between the various branches of the profession, and such natural flexibility of response must be preserved. The second danger is delay. The numbers of doctors are increasing so rapidly that, apart from the obvious risks of overcrowding to the profession itself, doubts must arise whether the country ought to be spending its resources on training so many students—not in some years' time but this year and next. Even now deans of medical schools might well warn prospective students that competition for the more attractive posts is much keener than formerly—no bad thing—and also that to find any opening at all may be a competitive affair by the time they have qualified in six years' time. If the last six years may be taken as a guide to the next six years, and medical and general populations of England and Wales[2] estimated accordingly, the student starting his course this year and qualifying in 1960 will find only 800 people per doctor instead of the present 900.

[1] See *Supplement*, p. 2.
[2] *External Migration*. Studies on Medical and Population Subjects, No. 6. General Register Office. H.M.S.O. 1953.

RETICULOENDOTHELIOSIS IN CHILDREN

The main, and often the only, justification for reporting a single case of an undiagnosed or hitherto undescribed condition is that similar cases may be recorded over the years. Eventually a clinical picture emerges sufficiently well defined to merit a name—usually eponymous, but this may be an advantage when aetiology or pathology is obscure. The syndrome associated with the names of Hand, Schüller, and Christian was evolved from descriptive case reports over a quarter of a century, starting in Philadelphia in 1893 with Hand's original description,[1] being embellished by Schüller's cases in Germany reported in 1915,[2] and returning to America for Christian's major contribution in 1919.[3] At first thought to be localized to the skull and characterized by the triad of proptosis, diabetes insipidus, and radiological changes in the cranium, it is now appreciated that the condition is often more generalized and that the spleen, liver, lymph nodes, skin, lungs, and other parts of the skeleton may be implicated. The disease usually starts during the first decade of life and runs a variable course; but it has been described in adults, with a more favourable prognosis and with spontaneous regression and disappearance of the easily seen bone changes. The characteristic histological finding is localized areas of macrophage infiltration containing multinucleated giant cells loaded with cholesterol. Hence the condition has been termed lipophagic granulomatosis and, because of the associated xanthomata in the skin, was at one time classified with the xanthomatoses.

More recently another syndrome, associated with the names of Letterer[4] and Siwe,[5] has been recognized. This condition is characterized by a sudden widespread overgrowth of reticuloendothelial cells in the lymph nodes, spleen, liver, and marrow. The histological picture differs from that in the Hand-Schüller-Christian syndrome, the lesions being more diffuse and both giant cells and lipid scanty. Clinically the Letterer-Siwe syndrome is an acute fulminating illness of infants with fever, necrotic lesions of the mouth and pharynx, otitis, cutaneous haemorrhages, and a rapidly progressive anaemia. The picture is reminiscent of an acute leukaemia, but because of the septicaemia-like course it has been called acute infectious reticulosis, although there is little to indicate an infective aetiology. Some patients show features of both syndromes, with fever, lymphadenopathy, petechiae, anaemia, hepatosplenomegaly, and arthritis, and patients with the Hand-Schüller-Christian syndrome may present in the terminal stages with all the features of the Letterer-Siwe syndrome.

Yet more recently a third condition called eosinophilic granuloma of bone has been described.[6,7] This usually occurs in late childhood or early adolescence, and is characterized by tumour-like destructive swellings of bone, often single but sometimes multiple. A low-grade pyrexia and leucocytosis may be associated. The histological evidence suggests that these three conditions are variants of a single disease entity—rapidly fatal in infancy (Letterer-Siwe disease), chronic but liable to acute exacerbations in early childhood (Hand-Schüller-Christian syndrome), and fairly benign in later childhood and early adolescence (eosinophilic granuloma).[8]

The effect of treatment is difficult to assess because of the variable course of the disease. Eosinophilic granuloma and, in its more benign form, Hand-Schüller-Christian syndrome show improvement with *x*-ray therapy. In the more acute type blood transfusions, *x* rays, nitrogen mustard, and antifolic acid drugs have been used with more limited success. The Letterer-Siwe syndrome is usually rapidly fatal, although Aranson[9] reports recovery in one infant after treatment with streptomycin. More recently Bass and her colleagues[10] have described the response of five cases to cortisone and A.C.T.H. One infant with the Letterer-Siwe syndrome showed no improvement, but in four children with the Hand-Schüller-Christian syndrome there was regression of the splenic and lymph-node enlargement, remission of fever, and great improvement in their general condition. In one child whose state was similar to that seen in Letterer-Siwe syndrome A.C.T.H. proved life-saving. This type of response is seen in other conditions, such as acute lymphatic leukaemia, after cortisone or A.C.T.H. therapy, but is unfortunately short-lived. Similarly in the Hand-Schüller-Christian syndrome the improvement was only temporary in one case and the child eventually died. In the others hormonal treatment seemed to tide the children over an acute phase and allowed them to live long enough for a spontaneous remission to be manifest.

1 *Trans path. Soc., Philadelphia*, 1893, **16**, 282.
2 *Fortschr. Röntgenstr.*, 1915, **23**, 12.
3 In *Contributions to Medical and Biological Research*. New York. 1919.
4 *Frankfurt Z. Path.*, 1924, **30**, 377.
5 *Z. Kinderheilk.*, 1933, **55**, 212.
6 Otani, S., and Ehrlich, J. C., *Amer. J. Path.*, 1940, **16**, 479.
7 Lichtenstein, L., and Jaffe, H. L., *ibid.*, 1940, **16**, 595.
8 Mallory, T. B., *New Engl. J. Med.*, 1942, **227**, 955.
9 *Lancet*, 1951, **1**, 889.
10 *Amer. J. Dis. Child.*, 1953, **85**, 393.

POST-OPERATIVE CHOLECYSTITIS

The surgeon often alleges most uncharitably that the worst place for a patient to have his peptic ulcer perforate is in the hospital ward of his physician colleague. However, he is not above criticism himself in overlooking the incidental surgical catastrophes which may infrequently occur in the immediate post-operative period. Of the hazards of the acute peptic ulcer, bleeding or perforating, he is well aware, and acute appendicitis may be obvious enough not to pass for long unrecognized. But there is one post-operative abdominal emergency of which he is likely to be unmindful—namely, acute cholecystitis. There is nothing unusual in the clinical features of the disease to mislead him; the site and character of the pain and tenderness follow the usual pattern: it is only the timing which is so unexpected. Subhepatic abscess, subdiaphragmatic pleurisy, or a blown duodenal stump are diagnoses which may first present themselves, but this complication is by no means peculiar to abdominal surgery. In only six of Glenn's seventeen cases of this complication did the cholecystitis follow intraperitoneal operations,[1] and in three of the

1 *Ann. Surg.*, 1947, **126**, 411.
2 Ibid., 1952, **135**, 863.
3 Schwegman, C. W., and DeMuth, W. E., *Surg. Gynec. Obstet.*, 1953, **97**, 167.

six recorded by Sparkman[2] the abdominal parietes were not involved. A more recent communication[3] has listed seventeen cases collected over a period of rather more than twenty years from the records of the hospital of the University of Pennsylvania. There were three deaths in this series and in each of them the diagnosis was established only at necropsy. Perforation of the gall-bladder occurred in four patients.

Perhaps during the period of anaesthesia and of the fast that usually follows the bile becomes stagnant and viscid. When later the gall-bladder is vigorously stimulated in response to the taking of food, obstruction and inflammation ensue, especially in the presence of stones. Certainly in a significantly high proportion of cases the first symptoms occur within 48 hours of the resumption of feeding. There can be no easy way of anticipating this complication. Even the palpation at laparotomy of what seems to be a normal gall-bladder is no guarantee against its later acute inflammation. But clearly surgeons should remember acute cholecystitis as an uncommon, though none the less serious, complication following operations for completely unrelated disease.

DIVERSITY IN DEVELOPMENT

In the half-century that has passed since the discovery of Mendel's work, Mendelian inheritance has been demonstrated so abundantly in living organisms that the chromosomes within the cell nucleus are apt to be regarded as the sole means of inheritance. Yet it has long been known that the chloroplasts of green plants are always derived from pre-existing plastids, and consequently their inheritance does not follow the Mendelian laws. In most flowering plants they are handed down to the next generation only from the female parent. More recently a few instances of such extranuclear inheritance have been found in micro-organisms. These are favourable subjects for genetic study, and, as Boris Ephrussi has shown,[1] two distinct types of cytoplasmic inheritance are now known.

In one type—for example, the plastids of green plants and the "killer" character of *Paramecium*—the characters in question are determined by autonomous particles in the cell cytoplasm, which are irreplaceable if lost; and specific genes in the nucleus are required for the reproduction or for the physiological activity of the cytoplasmic particles. In the second type of cytoplasmic inheritance, shown by antigens in *Paramecium*, the characters in question depend on the action of nuclear genes, whose manifestation is controlled by the cytoplasm, which is itself influenced by the external environment. In other words, a cytoplasmic character permits the expression of one particular gene out of a number present. There is no evidence that in this type of cytoplasmic inheritance discrete extranuclear particles are involved, and it seems more probable that under the influence of different environmental conditions, such as different temperatures, alternative but interacting reaction chains within the cell give rise to alternative stable cytoplasmic states.

These phenomena are interesting in themselves, but they take on a greater significance when compared with the process of differentiation into organs and tissues that is seen during the development of a living organism. Ever since the establishment of the chromosome theory it has been apparent that differentiation must originate in the cytoplasm. In no other way can differences between different cell-lineages arise, since mitosis distributes an identical set of genes to every cell. However, although genetically alike, the nuclei of different tissues may be functionally different. Indeed, it was long ago suggested that development consists in the orderly activation of different sets of genes in different cell-lineages. This is a remarkable parallel with the inheritance of antigenic types in *Paramecium*, where different cytoplasmic conditions call forth the activity of different nuclear genes. But, even if this is the mechanism of differentiation, there still remains the fundamental question of what initiates the cytoplasmic diversity during development. It is in the attempt to answer this question that profound differences of opinion exist at the present time.

Most geneticists favour the idea that the initial cytoplasmic diversity results from environmental stimuli external to the cell. The cytoplasmic diversity is thought to be similar in origin to the antigenic diversity brought about in *Paramecium* by the action of nuclear genes whose manifestation is controlled by the cytoplasm, this in turn being influenced by external stimuli. This hypothesis enables all cytoplasmic diversity (apart from structures known to be autonomous, such as the plastids) to be attributed to the functioning of different nuclear genes in different environments. But Ephrussi expresses a view which is revolutionary to most geneticists. He suggests that the initial cytoplasmic asymmetry of the egg cell reflects an underlying fundamental asymmetry at the molecular level. Furthermore, he thinks that this is inherent in the cytoplasm in the same way as the autonomous particles responsible for the "killer" character in *Paramecium*. Indeed, he goes so far as to suggest that the most fundamental characters of living organisms are inherited in the cytoplasm, and that the nucleus is concerned chiefly with the more superficial differences between individuals. Ephrussi's book is clearly written and he develops his ideas with great skill. Its appearance is salutary and it will give cause for thought on one of the most fundamental problems of biology.

THE FEEBLE-MINDED

The total number of mental defectives now under institutional care in England and Wales stands at 56,629. This figure includes 5,100 on licence, but excludes 2,385 in accommodation not vested in the Minister.[1] The number of patients awaiting admission in 1952 was estimated at 9,000, and of these 3,527 were considered to be urgent cases. Out of the latter figure some two-thirds were described as "low-grade children." Mental defectives occupy quite a large proportion of the total hospital beds in the country, and the long waiting-list is a serious

[1] *Nucleo-cytoplasmic Relations in Micro-organisms.* Oxford, 1953.

[1] Report of the Ministry of Health for 1952. Part I.

problem; indeed, it has been referred to by the Minister as "problem No. 1." For the many medical officers of health and others concerned with making the best use of the beds available it will be some consolation to know that the first new hospital to be built in this country since the war is to be devoted to mental defect. On the other hand, it should be noted that 1,921 existing beds are out of use principally owing to shortage of nurses. In the present difficult circumstances the lack of adequate statistical information about the mental deficiency service is unfortunate, the previous reports of the Board of Control being now replaced, so far as mental deficiency is concerned, by a few lonely paragraphs in the general report from the Ministry of Health. The survey by Drs. N. O'Connor and J. Tizard published elsewhere in this issue is therefore welcome. It provides, together with the other information available, a basis for taking stock of the problem of the institutional defective. It also poses the questions whether we are making the best possible use of the existing hospital facilities, and whether enough thought has been given to the possibility of returning some of the long-stay cases to the community.

To those familiar with the problem it will not come as a surprise to learn that over half the patients in mental deficiency hospitals are classed as feeble-minded or that the average intelligence quotient in young adults confined in these institutions is above 70. The reason usually advanced for the continued detention of these patients is that they constitute a "social problem" group. In fact the survey suggests that social problem cases make up only a small proportion of the total. The spread of the intelligence and character of these individuals who have been classed as mentally defective overlaps very widely with that of the general population. Is the fact that a small proportion of patients certified as mentally defective are "difficult" an adequate reason for detaining for an indefinite period others who might become so? Unfortunately the survey does not provide information about the proportion of the total effort devoted to the care of the mental defective which is spent directly on social rehabilitation, though the figures of patients on licence have an indirect bearing on this. A survey devoted purely to this aspect of the problem would be certain to yield valuable results. Meantime it is already apparent from this survey and from previous work reported by the authors that a high proportion of patients in mental deficiency institutions are potentially employable in building, in factories, or in agriculture. A good case has now been made out for the employment of additional experienced social workers or rehabilitation officers in the mental deficiency hospitals specifically for the purpose of placing these patients in suitable employment.

HEALTH HAZARDS IN THE CHROMATE INDUSTRY

Chrome ulceration of the skin or of the nasal mucous membrane has for many years presented a serious industrial problem in every country where chromates are made or used. One of the earliest reports of skin lesions in the form of large penetrating ulcers of the hands came from Scotland in 1827, and in 1902 the discovery in England by Sir Thomas Legge of a high incidence of perforated nasal septa among workers in a plant producing bichromate led to the setting up of a special code of regulations for the industry. Conjunctivitis, congestion of the throat, bronchitis, and acute toxic symptoms related to the digestive organs and the kidneys have also been noted as specific effects of exposure to chromates, but it is only rather recently that they have been indicated as a probable cause of lung cancer. The first report came from Germany in 1932 and was soon followed by many more, though neither the complete diagnosis of the neoplasm nor its connexion with chromate exposure was always indisputable.

The steadily growing suspicion of a carcinogenic hazard led the representatives of the chromate industry to request the Public Health Service of the U.S.A. to undertake an extensive inquiry into the problem, and the results have now been published.[1] The extent of the problem there can be judged from a comparison of the incidence of lung cancer in chromate workers with that in the general population, as exemplified in an *x*-ray survey of over 500,000 persons in Boston in 1949–50. This showed an incidence in the 897 chromate workers 32 times that of the Boston population at the age of 60–69 years, and 325 times as great at 40–49 years.

In Great Britain the problem of chrome ulceration has been met by statutory control, including periodical medical examination of workers in nearly all branches of the chromate industry. Most of the cases notified now are associated with chrome plating; the notifications from chrome tanning, dyeing, and finishing, for which Welfare Orders were made in 1918, have amounted to only two in the past five years. In 1951 there was an increase in all cases of chrome ulceration over those notified in 1950; this was largely accounted for by 80 cases occurring in the manufacture of bichromates.

There is certainly no such prevalence of lung cancer here as that indicated in the U.S.A. investigation. An inquiry in 1951 among 724 workers in the chromate-producing industry of Great Britain revealed only one case, a figure too small for a definite conclusion. It was then pointed out that the British process differs from that of both Germany and the U.S.A. in that the residue from the leaching tanks is not, in Great Britain, dried and crushed and used as a filler but is discarded in a moist condition and carried to dumps outside the factory. The residue, when crushed and recirculated, as is the practice in Germany and America, contains certain acid-soluble, water-insoluble chromium compounds, to which suspicion is directed in the U.S.A. report, though whether they are directly carcinogenic could not be established. The report recommends further research on the effects of all chromium compounds and, in the meantime, periodic *x*-ray examinations of all workers in the chromate producing industry.

[1] *Health of Workers in Chromate Producing Industry*, Federal Security Agency. Public Health Service, 1953.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

BLOOD GROUPING

BY

A. E. MOURANT, D.M.

Director, Blood Group Reference Laboratory, the Lister Institute, London

Persons whose blood group needs to be known for medical reasons fall into three classes: blood donors, blood transfusion recipients, and pregnant women.

Blood donors are almost exclusively grouped by the National Blood Transfusion Service. Relatively small numbers are grouped by the Greater London Red Cross Blood Transfusion Service and by individual hospitals. It practically never happens that a donor has to be grouped or a sample taken for grouping other than at a large transfusion centre of some sort.

Apart from the most severe obstetrical haemorrhages, and uncontrollable haemorrhages due to accidental trauma, transfusions are never carried out away from hospitals. Such obstetrical and traumatic cases will, in general, be transfused with group O, Rh-negative blood by "flying squads" without preliminary grouping. Hence blood grouping of recipients is always carried out in hospitals or is done for them by the laboratories of the National Blood Transfusion Service. The same applies to the direct matching between the blood of donors and recipients.

The blood grouping of pregnant women is carried out for antenatal clinics by hospital laboratories or by the National Blood Transfusion Service, and the necessary samples are taken at the clinics. When a pregnant woman is not attending a clinic, her own doctor should arrange for the performance of the necessary tests either at the local hospital laboratory (as for other pathological tests) or at the Regional Blood Transfusion Centre. Local arrangements vary, but information about them can be obtained from the regional transfusion director or from the medical officer of health.

Collection of Specimens

For the tests a sample of blood of at least 5 ml., and preferably 10 ml., should be taken with a dry sterile syringe into a dry sterile tube. This relatively large volume is needed in order to supply enough serum for antibody tests. If the necessary syringe and tube are not available it is best to use a Behring venule* prepared without anticoagulant or preservative. It is perhaps worth repeating that to release the vacuum in a venule the needle should be bent further away from the axis of the tube, not brought into line with it. The alternative of a syringe kept in alcohol carries the well-known risk of transmitting homologous serum jaundice, but if it is used it should be rinsed several times in sterile physiological saline.

If a woman is found to have an abnormal antibody in her serum it may be necessary to test specimens from her husband and in some cases from their children. The specimen from the husband should consist of 2 to 5 ml. of whole clotted blood. Specimens from children may have to be obtained by pricking the heel, ear-lobe, or finger with a triangular needle. At least 10 drops of blood should be taken into a small dry sterile tube; some laboratories may, however, ask for such specimens to be taken into 3.2% sodium citrate or other anticoagulant.

Where there is a possibility of haemolytic disease of the newborn, it is necessary to carry out blood grouping and other tests on the blood of newborn infants. For certain of the tests (especially the haemoglobin estimation) a cord-blood sample is essential. As soon as the cord is cut and tied, 5 ml. of blood is taken with a dry syringe (or venule) from the maternal end of the cord and put into a tube containing dry oxalate or heparin. It is important to use a dry tube so as to obtain an accurate result in the important haemoglobin determination. A separate specimen without anticoagulant is needed for serological tests. Capillary blood from the infant is useless for haemoglobin tests if they are to be of prognostic value in haemolytic disease of the newborn. The blood should be taken by piercing the umbilical vein in the tied cord as though it was a subcutaneous vein. Any attempt to obtain blood from the open cut end of the cord is apt to lead to contamination with Wharton's jelly or even with maternal blood.

*See the article by Dr. Martin Hynes on "Dispatch of Specimens," published on October 17, p. 876.

The ABO Blood Groups

The only tests which are performed on all (or nearly all) blood samples are those for the ABO groups and for the Rh factor or factors.

The ABO groups depend upon the existence on the red-cell surface of two substances or antigens known as A and B. Chemically they are very closely similar polysaccharides of high molecular weight, and the only clearly defined difference between them is that shown in agglutination reactions of the kind described below. All human red cells are classified into four groups—A, B, O, and AB—according to the presence on them of either, neither, or both of these antigens. These are detected by tests carried out with certain human sera containing antibodies in solution. When red cells carrying the antigen A are mixed with a serum containing anti-A, the surface properties of the red cell are altered in such a way that the cells stick to one another or agglutinate into large clumps. Cells carrying the antigen B react similarly with a serum containing anti-B. The antibodies in question are present in normal human sera: each serum contains all those antibodies which will not agglutinate the red cells present in the same blood. Thus anti-A testing serum is derived from group B blood, and anti-B serum from group A blood. The above facts are summarized in the Table.

Name of Blood Group	Antigens on Red Cell	Red Cell Reaction with Anti-A	Red Cell Reaction with Anti-B	Antibodies in Serum
O	–	–	–	Anti-A and anti-B
A	A	+	–	Anti-B
B	B	–	+	Anti-A
AB	A and B	+	+	–

When any blood is tested it is necessary not only to examine the red cells by means of standardized anti-A and anti-B sera but also to test for the presence of anti-A or anti-B antibodies in the serum by the use of red cells known to be of groups A and B. Tests are in general carried out by mixing small quantities of the appropriate sera and red-cell suspensions in glass tubes. The mixtures are kept at room temperature for two hours before being examined microscopically. A working description of the technique of blood grouping is beyond the scope of this article and is given in the *Medical Research Council War Memorandum* No. 9.

In deciding what blood is suitable for a given recipient, the principal consideration is the absence of reaction between

the red cells of the donor and the serum of the recipient. Since high titres of antibody in the serum of the donor may also on rare occasions cause trouble, it is desirable always to give a recipient blood of his own group. In an emergency, however, group O blood can without great danger be given to anyone.

The Rh Factor

Every person, whatever his or her ABO blood group, is either Rh-positive or Rh-negative—that is, the red cells either contain or do not contain an antigen known as the Rh factor, or, more precisely, as the D antigen. The corresponding antibody, anti-Rh or anti-D, is not normally present in the serum of D-negative persons, but such a person, if transfused with D-positive blood or, in the case of a woman, if she bears a D-positive child, may become immunized by the D factor, so that an anti-D antibody develops in the serum. A subsequent transfusion of D-positive blood will then give rise to haemolysis and to a severe reaction. About 50% of D-negative persons receiving a single transfusion or course of transfusions of D-positive blood will become immunized. Of D-negative women who bear D-positive children, about 1 in 20 becomes immunized. It is thus important that D-negative persons, especially women, should, if transfused, receive only D-negative blood. The serum of D-negative persons who have been immunized to the D antigen will, under suitable conditions, cause *in vitro* agglutination of D-positive red cells. Such pathological sera are used in Rh blood-grouping of transfusion donors and recipients.

It is desirable also that the blood of all pregnant women be tested for Rh as well as for ABO. Two objects are in view: one is to be ready to transfuse should there be severe haemorrhage at the time of parturition; the other is so as to recognize the presence of immunization and so to be prepared for the birth of an infant with haemolytic disease. Every woman who is D-negative should therefore have her serum tested for the presence of anti-D.

Rh-testing procedures are complicated by the fact that the Rh factor is a complex entity, though most of its details have very little direct bearing on clinical medicine. Whatever other antigens may be or may become involved in the situation, however, all transfusion recipients who are negative for the D antigen, and likewise all pregnant women who are D-negative, are liable to develop anti-D. Thus a test of the red cells of all such persons should be made with anti-D serum: for nearly all purposes this single test is the only one that need be performed on the red cells.

The tests on donors are less simple and the extra tests mainly concern two other antigens of the Rh complex. known as C and E. Most D-positive bloods contain either or both of these antigens as well as D, and D-negative persons who develop anti-D are liable to make anti-C or anti-E as well. The transfusion of blood from a donor who is D-negative but C-positive or E-positive will of course be dangerous to such a recipient. Thus it is necessary after selecting D-negative donors with an anti-D serum to eliminate the relatively rare ones who have the C or the E antigen, by further testing with anti-C and anti-E sera. There is another antigen which may give rise to difficulties in the testing of donors, recipients, and mothers. It is known as D^u, and persons who have it are liable to appear D-positive when tested with some sera and D-negative with others. When the possibility of its presence is realized this is easily confirmed or disproved. Persons who are D^u-positive may be treated for clinical purposes as D-positive.

Tests for Rh antibodies in sera are carried out by means of red cells of known Rh groups. The sera of persons who are to be transfused may contain any of the antibodies already mentioned (anti-A, -B, -C, -D, -E), as well as other rarer ones which need not be described here. Even Rh-negative blood may react with some of these. It is therefore necessary before any transfusion to test the compatibility of the red cells of each donor with the serum of the recipient.

The methods of Rh testing and of direct matching are described in "The Rh Blood Groups and their Clinical Effects," by P. L. Mollison, A. E. Mourant, and R. R. Race (*Medical Research Council Memorandum* No. 27).

Planning of Blood Grouping

Only the principles and not the practice of blood grouping (including direct matching) are described in this article. It is of the utmost importance that it should be realized both by those who do blood grouping tests and by those who without adequate training may wish to do them, that, of all pathological tests, blood grouping carries the greatest responsibility: it is the one kind of test in which a single error may lead directly to the death of a patient. Thus no one who has not received a course of training in blood grouping should ever attempt to carry out such a test. Under emergency conditions, when the temptation to do the test will be the greatest, the danger of error will also be greatest. Rather should an irate pathologist be awakened from his bed and compelled to travel many miles to the hospital. Any doctor who is going to be completely isolated from laboratory facilities should obtain training in blood grouping just as he would in emergency surgery.

Instruction of house-officers and others in routine blood grouping and direct-matching techniques can be arranged through any regional transfusion director. While the house-officer untrained in blood grouping must never attempt to carry out the test, it is important that both he and his seniors should have an idea of what is involved in blood grouping and direct matching so that they can collaborate effectively with those who are doing the tests. It is agreed by most pathologists that adequate blood grouping and cross-matching tests require incubation for two hours. Hence, in the case of planned operations which may involve transfusion, a sample of the patient's blood should be sent to the laboratory well in advance of the operation—preferably some days before. Many laboratories have special arrangements for emergency grouping and direct matching by special methods which take about half an hour. Where such provision has been made emergencies are only very rarely so acute as to demand the transfusion of group O, Rh-negative blood into an ungrouped patient. Many so-called emergencies can be foreseen, and it must be realized that with emergency direct matching the possibilities of error, though slight, are appreciably greater than in normal tests.

In certain classes of surgery it is necessary that there should be available for each patient large quantities of blood which may or may not prove to be needed. In some cases the same bottles can be matched direct against the blood of several patients, but to save opening of bottles several times, and also possible confusion between the bottles intended for different patients, it is important that the routine of notification, sampling of patients' bloods, testing, and labelling of bottles should be carefully planned by consultation between the surgeon and the pathologist.

Interpretation of Rh Blood-group Tests

Cards bearing a statement of the ABO and Rh group are given to blood donors, to most pregnant women, and to a few transfused persons. On cards given to Rh-negative (D-negative) persons in the latter two classes there may also be a statement that the serum contains anti-Rh antibodies. A woman who knows that she is Rh-negative is likely to approach her doctor for information and advice about the possible effects on her children. If the husband or prospective husband is known to be Rh-negative as well, complete reassurance can be given. The shortage of testing sera is such that it is only in exceptional cases that a special test of the husband's blood can be justified for this purpose. In an Rh-negative woman who has never had a blood transfusion, the occurrence of clinical haemolytic disease of the newborn affecting a first pregnancy is practically non-existent, though slight immunization of the mother may occur. In the second pregnancies of Rh-negative women married to Rh-positive

husbands about 1 in 20 foetuses will suffer from haemolytic disease. The proportion of affected infants will increase somewhat with successive pregnancies. Once a woman has become immunized to the Rh factor all her subsequent Rh-positive children will suffer from haemolytic disease. If her husband is homozygous Rh-positive—that is, if he has received the Rh or D factor from both of his parents—then all the children will be Rh-positive (and therefore affected by the disease), whereas if the husband is heterozygous Rh-positive (having received the Rh or D factor from one parent only and the Rh-negative or d factor from the other parent) then any subsequent child has equal chances of being Rh-positive and affected or Rh-negative and healthy.

If any child of the couple is known to be Rh-negative this shows the husband to be heterozygous. Tests carried out on the husband's blood alone can never show with complete certainty whether he is homozygous or heterozygous, but they can do so with a high degree of probability. Where, therefore, an Rh-negative woman has become immunized to the Rh factor and there is a desire to increase the family, the Rh genotype of the husband should be determined. The necessary test requires the use of scarce and valuable kinds of antisera and can be carried out only at regional transfusion centres and a few other laboratories.

The above paragraphs have been written as though the Rh or D factor were the only one responsible for haemolytic disease of the newborn. In rare cases other Rh antigens, the A and B antigens, and antigens of other blood-group systems may be responsible. Where such cases are detected the medical officer in charge of the testing laboratory will readily give the necessary advice on such matters as prognosis for future pregnancies.

It is well known that Rh-negative persons should, in general, be transfused only with Rh-negative blood. If they have become immunized to the Rh factor by pregnancy or transfusion, any further transfusion of Rh-positive blood may be fatal. It is unnecessary to alarm such persons regarding their "condition," but they must be warned always to carry their blood-group cards and to proffer these when entering hospital for any reason.

Next article on Clinical Pathology.—"Investigation of Outbreaks of Infection," by Dr. R. E. O. Williams.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1. or from booksellers.

OPHTHALMIC SURGERY IN INDIA

SOME ENCOURAGING FEATURES*

BY

J. N. TENNENT, M.B., B.Sc., F.R.F.P.S., D.O.M.S.

Ophthalmic Surgeon, Glasgow Royal Infirmary

A visit to India was organized in 1951 by Dr. R. U. Hingorani, an Indian ophthalmic surgeon practising in London. It was primarily a pleasure trip, a sight-seeing tour, but as the party was composed mainly of medical consultants and their wives, with a core of European ophthalmic surgeons, medical conditions aroused most interest, especially the efforts made to remove that great affliction of India, disease of the eye.

The amount of suffering in India is appalling, most of it preventable. This is not surprising, for there is a great shortage of trained medical personnel. A recent estimate states that there is only one trained doctor for every 10,000 of the population, as against one for 900 in Great Britain. In addition, the doctors are poorly distributed, being congregated mostly in the towns. Facilities for the application of modern scientific medicine are lacking, and there still exists a good deal of native prejudice. Quacks abound. Some have a useful knowledge of Indian herbs and a skill in their application, passed on from father to son, but many indulge in superstitious practices concerned with the exorcizing of demons or the placating of evil spirits, practices which are often both crude and cruel. A man in any walk of life may pick up something about cataract extraction, set up in practice, and soon acquire a reputation as an eye specialist. Government intervention is not yet considered necessary, but it must come sooner or later.

Living Conditions

Poverty abounds. Most of our party had to revise their conception of the meaning of the word "poverty." In some of the refugee camps human beings were seen with scarcely a roof to cover their head. In the village huts we visited there was sometimes little else than some cooking utensils, a few fowls, and a receptacle to hold the family's supply of rice for the year.

With poverty go overcrowding and malnutrition. In the city of Bombay some 200,000 people sleep on the streets. This is partly a matter of choice owing to the heat, but is also partly due to the fact that many have little more than an accommodation address, a room which 20 or more people use to hold their worldly possessions while they eat and sleep on the streets.

Rice is the staple food; indeed, it is almost the only one, with resulting lack of balance in diet and deficiency disease. The fields given over to the cultivation of rice may provide excellent breeding grounds for mosquitoes and the spread of malaria.

A feature of Indian life that strikes the stranger forcibly is the lack of adequate attention to sanitation. Large cities like Calcutta still have open sewers in the streets, and cows are allowed to wander about unmolested even in the main thoroughfares. Some of the villages we visited were quite unprovided with streets, lighting, and sanitation, so that the spread of epidemics in the time of the monsoons can scarcely be avoided.

Finally, there is still to be found the secluded life of many women living in purdah. This system intensifies the lack of medical attention for women and children, and thus leads to needless suffering. A recent estimate gives the expectation of life for an Indian woman as 27 years as against 67 in Great Britain.

It is not my purpose to dwell on the lethargy, poverty, ignorance, and superstition of India. Rather do I wish to draw attention to some signs of an awakening to the need for action which is going on, particularly among Indian doctors. The Government also is becoming more alive to the need to do something to remove the great scourge of disease from India.

The most serious medical affliction is tuberculosis. Next comes eye disease; and here most authorities agree that at least 90% of it is preventable. I shall refer to one or two encouraging features in the ophthalmological field.

The Gandhi Eye Hospital

The Gandhi Eye Hospital is in Aligarh, a Moslem university town of 140,000 inhabitants, in the State of Uttar Pradesh (formerly United Provinces), 84 miles south-east of Delhi. The hospital has 100 beds, and plans to increase the number to 250. It began in 1928 as the private clinic

*A lecture delivered in the Department of Ophthalmology, University of Glasgow, on May 14, 1952.

of a public-spirited Indian, Dr. Mohanlal, who developed the work on a voluntary basis, and in 1941 handed over the assets to a public trust. Since then the hospital has been rebuilt, partly by voluntary subscription and partly by Government grant, and now stands on a new site covering 16 acres. With only 100 beds, extra accommodation has to be found sometimes for as many as 300 patients; and in winter some 500–600 patients may have to be provided for by means of extra tentage. Winter is the best time for cataract operation. In summer it is too hot, patients are restless, there is a constant battle against flies, and infection is more likely. In summer patients with diseases such as trachoma are more likely to find their way to the operating theatre. The hospital building is new and is provided with much up-to-date and expensive equipment. There are separate departments for refraction, radiotherapy, orthoptics and optical dispensing.

The staff consists of one chief medical officer, four ophthalmic surgeons, three assistant ophthalmic surgeons, two refractionists, one laboratory assistant, and several compounders, theatre assistants, and ward boys. Female nurses are conspicuous by their absence, for nursing is regarded as an unsuitable occupation for a girl of education or social standing.

The following figures show the yearly amount of work carried out:

New patients	20,000
Total patients	80,000
Refractions	5,000
Operations	6,000

The patients bring their own food and linen, with someone to look after them. Those who are too poor (10%) get free food. Private patients are provided for; these pay 100 rupees (£7 10s.) for treatment and lodging.

The cataract operations in the height of the season number 60 a day. One surgeon generally operates, with three or four tables. The usual mode of extraction is the intracapsular.

The hospital is intended to be the centre for postgraduate study and for research. The most significant feature of this hospital, however, is its interest in rural work and its use of the mobile eye hospital. To appreciate the significance of this it is necessary to know something about the district in which the hospital is situated.

Uttar Pradesh is one of the most important States of India. It is right at the heart of the country—Hindustan of the old Moslem chronologers. It includes important cities like Agra, Aligarh, Lucknow, Allahabad, and Benares. Together with Delhi on the west and Patna on the east, it represents the area of the dawn of Indian history. There Brahminism took form; Buddha was born, preached, and died; the Mogul Dynasty had its most brilliant period; the Indian Mutiny took place, with the establishment of British dominion; and there also New India has more recently taken shape. The State has an area of over 106,000 square miles and a population of some 60 millions.

Before 1930 the facilities for the treatment of eye disease in this Province were meagre indeed. Eye cases tended to find their way to the district general hospitals, the State being divided into 51 districts. There they were seen by the civil surgeon, and treatment was mostly operative. At Agra and Lucknow there were medical colleges, each with an eye department, and at Allahabad there was a hospital where a limited number of eye patients were treated. In addition, in winter a well-known Indian eye surgeon used to hold eye camps where mass surgery was done. The great majority of eye patients were at the mercy, however, of village quacks or couchers.

Around 1930 in Uttar Pradesh there developed two eye hospitals, one at Aligarh and the other in Khairabad. This latter hospital has also recently been rebuilt, and is now at Sitapur. Both these hospitals set out to do village work, and in 1949 the Government approved of a State-wide scheme with them as base hospitals.

In the area allotted to the Gandhi Eye Hospital it is intended that in, say, 15 years each district will have an eye clinic in charge of a properly trained eye specialist. Meantime, however, a short-term policy provides for four mobile eye hospitals. Each of these will have 100 beds, a field operation theatre, and accommodation in tents for staff and patients. Except in the hill areas, work will be done mainly in winter. The hospital will visit one district for six to eight weeks and remain in one centre for, say, 20 days. There will be a permanent staff, with visits from the surgeon of the Gandhi Eye Hospital, and use will be made of Government medical officers and local eye specialists.

The proposed personnel will still be woefully short for such a vast area, but the step taken is considerable and is in the right direction. It will help to break away from outmoded and pernicious eye camps, which, while popular with the people and the Government, have not been run on scientific lines. It will provide for the treatment of eye disease apart from cataract. It will educate the people regarding the prevention and control of eye disease, develop an eye consciousness in school health administration, and break down much prejudice against scientific treatment.

At present eye disease and consequent blindness in the countryside are said to be increasing day by day, so this scheme is a welcome effort to tackle an enormous and serious problem.

Experience in Bombay Province

A well-known Indian ophthalmic surgeon has classified his colleagues into three groups: (*a*) mass surgeons, (*b*) scientific surgeons, and (*c*) occasional surgeons. That classification implies that mass surgeons are not scientific surgeons, and the statement was no doubt true when it was written. In recent years, however, there has been a growing concern in the highest quarters about mass-operation camps, and steps are being taken in some parts to place these camps on an irreproachable basis.

In Bombay Province, for example, the surgeons have become concerned about the advent of outsiders with a medical training, but no training in ophthalmic surgery, who stay for three or four days and conduct a large number of operations for cataract. The cases are then left in the hands of compounders and much sepsis results. In spite of their shortcomings such camps are welcomed by the people, who are often satisfied if they can see even a little again.

The ophthalmic surgeons in Bombay approached the Government to see what could be done, and at once received the challenge, "What can *you* do to help?" The outcome was the establishment of two camps yearly by the surgeons themselves—one in April and one in October—alternating between the northern and southern parts of the province.

A school or military barracks provides a suitable building for the requirements of the camp. When we visited the province in November one such camp had just finished at Pandharpur, and for some details I am indebted to Dr. Pradahan, of Poona, who took part.

The staff of this camp consisted of two senior surgeons, two assistant surgeons, three postgraduate students, and two additional surgeons from the district. One of the senior surgeons of Bombay was in charge.

An attempt was made to get all patients examined first by local Government doctors so that undesirable cases could be weeded out. When the camp began all the staff devoted the whole of the first day to seeing out-patients. Those with less than a certain standard (6/60 Snellen) were generally admitted. On the second day one-half of the staff operated in the forenoon while the other half saw patients; in the afternoon the order was reversed. Operations went on for four days and then stopped.

The patients were given a careful examination, attention being paid to teeth, lacrimal ducts, blood pressure, and urine,

and the usual dark-room investigation was done. On admission the patient was given a brisk purge; until operation the eye was washed and penicillin drops, 2,500 units per ml., were instilled three times daily. 5 ml. of milk was injected intramuscularly—a non-specific protein therapy which increases leucocytosis. On the operating-table penicillin drops were instilled and 50,000 units injected subconjunctivally in 0.5 ml. of solution before or after the operation. Sulphadiazine tablets were also given for four days. Forty-eight hours after the operation the eye was dressed; if it was satisfactory the other eye was left uncovered. The dressing was repeated every second day and dark glasses were given on the eighth day. Intracapsular extraction was generally done for immature and hypermature cataract; for intermediate types the surgeon used his own discretion regarding the best method of procedure.

This project is financed by the Government. Glasses are supplied free, lodging is free, and the patient's rail fare is paid if necessary.

The following is a brief summary of the work done and the results achieved:

Total No. of out-patients	3,372
" " " in-patients	845
" " " operations	1,084
" " " cataract operations ..	676

Of the 676 cataract operations, only 40 showed any post-operative complication, and only four eyes were lost—one from sepsis and three from intraocular haemorrhage. Such results would adorn the records of ophthalmic surgery anywhere.

A High Standard

The ophthalmic surgery is of a very high standard in the leading eye hospitals. In Bombay I had more time to see the hospital work than elsewhere, but members of our party had an opportunity of seeing similar work in Calcutta and Patna; and, as is well known, Madras has been an important centre of ophthalmic surgery for many years. The standard of cataract work in the leading eye hospitals in Bombay is very high indeed, and the results of the keratoplasty work are most encouraging. In a land where corneal opacities are so numerous there must be great scope for grafting, and it will expand in the near future if grafting material becomes more readily available. In Bombay research is being pursued with considerable success.

Eye surgery would seem to be handicapped at present by lack of personnel and lack of finance—both dependent, no doubt, on the general economy of the country. Another difficulty, and one which should be easier to overcome, is the apparent scarcity of surgical instruments of high quality. It should not be impossible to produce one or more Indian firms capable of manufacturing and maintaining ophthalmic surgical instruments adequate in quantity and quality.

Finally, it was a pleasure to meet with so many Indian colleagues, to discuss their problems, and to appreciate their work. There is still much to be done, and signs are not wanting that the magnitude of the task is appreciated and that a bright future lies ahead.

PRESENTATION TO PROFESSOR CHARLES SINGER

Professor Charles Singer has for many years been the leading historian in this country both of medicine and its allied sciences and of technology. When, therefore, the project was mooted of presenting him with a volume composed of a series of special contributions written by his friends and admirers, it met with an enthusiastic response. The responsible and difficult task of collecting and editing the contributions was undertaken by Dr. Ashworth Underwood, and to him must also be given the credit for arranging the various essays into groups having a similar theme or dealing with a definite period. The 90 contributors represent many countries, and the work has been published by the Oxford Press in two excellent volumes, and entitled *Medicine, Science, and History*. It was arranged that specially bound copies of the two volumes should be presented to Professor Singer at Fowey, which is fairly near his home, and on December 19 the presentation took place at the end of a luncheon which was given in his honour. Among those present were his talented wife, Mrs. Dorothea Singer, Professor Gordon Childe, Professor K. J. Franklin, Dr. F. A. Freeth, Mr. Affleck Greeves, Dr. C. T. Andrews, Mr. Douglas McKie, Dr. Ashworth Underwood, and Professor Singer's son and daughter. The occasion was to have been presided over by Sir Arthur MacNalty, but in his unavoidable absence Sir Zachary Cope deputized for him. A special menu card had been prepared which included a photograph of Professor Singer and also sketches of the four places

[George W. F. Ellis, Bodmin

Professor Singer receiving the presentation volumes from Sir Zachary Cope.

with which he had been most closely associated, while the different items on the menu had been given names which recalled many of the subjects on which he had written with authority. Dr. Underwood read out many messages of congratulation sent by friends who had been unable to make the journey to Cornwall. In making the presentation to Professor Singer, the chairman said that it was a unique occasion. Never before had any celebrated medical historian received in person such a noteworthy testimony of the high regard in which he was held by his contemporaries. He recalled that they were both alumni of St. Mary's Hospital medical school and that they had been house officers in the hospital together. In handing to Professor Singer the sumptuous volumes, Sir Zachary remarked that they were accompanied by the great respect, admiration, and affection felt towards him, not only by the whole body of contributors, but by a much wider circle of admirers over the whole civilized world.

Professor Singer, who was much moved by the occasion, said that it was the happiest day in his life. He commented on the factors which enabled him to accomplish what he had done. First the influence of his home, for his father was a great scholar and an erudite man, and from his earliest years he had lived in an atmosphere of learning. Among colleagues who had helped him he specially mentioned the late Professor Arthur Platt. He finally paid a glowing and affectionate tribute to his wife, Mrs. Dorothea Singer, who was not only a distinguished scholar in her own right but had inspired and helped him to an incalculable degree. This unity of endeavour was signally shown in his closing sentence: "We thank you from the bottom of our hearts."

Tributes were afterwards paid to their honoured guest by others who were present. Professor Singer is 77 years old.

Nova et Vetera

BIBLIOGRAPHY OF HARVEY

A Bibliography of the Writings of Dr. William Harvey, 1573–1657. By Geoffrey Keynes, M.A., M.D., D.Litt., F.R.C.S., F.R.C.O.G. Second edition, revised. (Pp. 79; illustrated. £2 10s.) London: Cambridge University Press. 1953.

Within living memory the art of bibliography has been refined far beyond anything previously attained. Certainly its recent practice by those with the suitable cultural and intellectual attainments, and, above all, with that indefinable thing called "judgment," has produced results which would have astonished their predecessors. Exact modern bibliography often enables the student to penetrate beyond the printed page to the very mind of the author treated. Among exponents of this art, Mr. Geoffrey Keynes has long been held in honour for the light that he has thrown on the life and work of such figures as Jane Austen, Donne, Sir Thomas Browne, William Blake, Hazlitt, John Ray, and Izaak Walton. This accomplished man has also applied himself to the work of William Harvey, who is in some ways an ideal subject for bibliography, since not a few of the editions of his several works are so rare that the number of surviving copies is approximately known and each copy located.

In 1928 Mr. Keynes produced a bibliography of Harvey in a very limited edition. It has long been out of print and a desideratum of scholars. This second edition, the scheme of which is faultless, is in even more sumptuous form. It follows the general lines of the first, but includes different illustrations, previously unrecorded editions, and a certain number of new facts. Of these the most interesting concern the printing and printer of the *De motu cordis*. It has always been a puzzle why Harvey should not have issued his great work in London, where there were many excellent printers, but at Frankfort-on-Main, with a young and not very competent printer, William Fitzer. The matter has been elucidated by Dr. Ernst Weil, who published his findings in 1944. They are linked with the life of Dr. Robert Fludd (1574–1637), a most peculiar figure who combined some understanding of the "new philosophy"—which we call "science"—with the wildest mysticism. The late Dr. H. P. Bayon threw some light on the relations of Fludd and Harvey. Mr. Keynes thus summarizes these researches:

> "It seems that Fludd from 1617 had his books published by Johann Theodor de Bry of Oppenheim, formerly of Frankfort. In 1619 the firm returned to Frankfort, and in 1626, when de Bry died, the business passed to Fitzer, who then took over the publication of books by Fludd. Harvey had many contacts with Fludd beginning in their student days at Padua in 1602, and is exceedingly likely to have been influenced by him in choosing Fitzer as his publisher. Fitzer's career from 1600 to his death in 1671 has been fully elucidated by Dr. Weil but does not further concern us here. The choice of Frankfort, however, was certainly unfortunate, since its distance from London made communication difficult, and it seems to be unlikely that Harvey ever saw any proof-sheets of his book. Had they come under his eye he would hardly, even in those days of bibliographical insensibility, have passed so many errors in so few pages. It is probable that when the first copies reached him he was displeased, and sent Fitzer a list of errata as soon as he was able. A minority of the surviving copies of the book contain an additional half-sheet of two leaves, the first of which carries a list of 126 corrections. Probably these leaves were added only to the remainder of the edition, after the greater part had been distributed—even so the *errata* list was not long enough; the Latin text edited by Mark Akenside for the College of Physicians in 1766 contains 246 emendations."

Anyone who has tried to read Harvey's handwriting will spare a sigh of sympathy for his printer. It is in the mode to ascribe many qualities to the great father of modern physiology, but the hero-worshipper who will credit him with a clear neat script has yet to emerge.

CHARLES SINGER.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Whither Anaesthesia?

SIR,—At the summer meeting of the Section of Anaesthetics of the British Medical Association at Cardiff the subject of the morning session was "A Return to Simplicity?" and I think that the general feeling was that this discussion was timely, if not overdue. Since that date the tendency has been to greater and greater complication.

From a perusal of papers published in the British and French medical journals and those read at the Royal Society of Medicine it would appear that one line of thought now runs as follows. The over-enthusiastic use of hypotensive techniques to provide a bloodless field for surgeons has forced into prominence accompanying dangers. In order to minimize these, it was suggested that hypothermia would reduce the basal metabolic rate, so that such blood supply as remained would afford adequate oxygenation of vital structures. Unfortunately, hypothermia induced by superficial cooling in patients who are sedated or lightly anaesthetized without complete relaxation results in a violent reaction, including shivering, etc., designed to keep the temperature up and to raise the B.M.R. In order to circumvent nature still further, it appears to be necessary to avoid surface cooling (in adults) and to effect the temperature drop by an extracorporeal arteriovenous shunt passed through a refrigerator. If this complicated technique is to be avoided an intravenous infusion of various "lytic cocktails" can be substituted. These may contain a great variety of drugs (some French workers use twelve), including at least two which have not yet been fully worked out as regards their pharmacological effects. It is hardly surprising that patients take a considerable time to recover from these varied assaults, and an impression is beginning to gain ground that pulmonary complications and paralytic ileus are more frequent than with orthodox techniques.

I would be the last to decry real research into anaesthetic methods capable of coping with, say, intracardiac surgery with a shut-off cardiac inflow, but these complicated techniques are being used on some patients undergoing routine surgery which can be dealt with by well-tried and simple methods. Surely the correct and scientific approach to any problem is to investigate it one step at a time. For example, if it is thought that intravenous chlorpromazine is likely to be a useful drug to diminish the B.M.R., to facilitate cooling, to potentiate anaesthetic drugs, or to minimize post-operative vomiting, then it (and it alone) could be added in a series of patients undergoing routine operations, all other anaesthetic and surgical factors being kept the same, so far as practicable, as with a previous controlled series. If significantly beneficial results follow, the optimum dosage could be worked out and the next step embarked upon. If, on the other hand, complications such as venous thrombosis were noted, they must either be overcome or the decision would have to be taken whether the advantages of the drug outweighed its disadvantages. As matters stand at present, groups of workers all over the country appear to be giving large numbers of drugs of diverse actions in various dosages, and in an infinite variety of permutations and combinations with such other procedures as induced hypothermia and hypotension. The results of small series of cases are then rapidly published in terms which are often obscure. For example, what are the definitions of ganglioplegic and neuroplegic drugs, and is artificial hibernation an accurate term when the differences between hibernating mammals and non-hibernators are considered? Is it any wonder that the student and, indeed, the experienced anaesthetist is becoming bewildered?—I am, etc.,

London, N.6. C. LANGTON HEWER.

Press Publicity

SIR,—What a silly and sanctimonious little piece was that contributed to your issue of December 19, 1953 (p. 1378), by Miss B. M. Willmott Dobbie. "Journalists, of course, have their living to earn." Surgeons, too, I fancy.

Of course, vulgar reporting of medical matters is to be deplored and is deplored by none more so than by responsible journalists. But part, at least, of the blame must be attributed to such superior persons as your correspondent who fail to co-operate in enabling journalists to present simply and factually the more remarkable achievements and advances in the art and science of medicine.—I am, etc.,

London, E.C.4. JOHN PRINCE.

Intra-arterial Transfusion

SIR,—It appears to me that the success of intra-arterial transfusion depends upon what is called the hydrostatic paradox, which states that "any quantity of water however small may be made to counterbalance any weight however great." This is brought about by the fact that in a liquid pressure is transmitted equally in all directions, and consequently the pressure on any given surface is proportional to the area of that surface. From this it follows that, if the pressure in a narrow artery is raised by the injection of fluid under pressure, the pressure in the wide aorta is in proportion to the differences of their sizes. This is considerable, even allowing for the loss of efficiency in the hydrostatic system occasioned by leakage into the arterial tree.

The repercussions of raising the intra-aortic pressure are manifold—perfusion of the coronary arteries, oxygenation of the tissues, take-up of blood from the venous bed, filling and emptying of the right heart, leading to increased efficiency of the cardiovascular system, etc.—and are amply illustrated in the reports of successful intra-arterial transfusion.

I submit, therefore, that, rather than continuous intra-arterial transfusion under pressure, it is more rational to apply intermittent intra-arterial injection until the take-up of blood from the venous bed is established in cases of shock, or from intravenous blood in cases of haemorrhage.—I am, etc.,

Northallerton. J. SHEGOG RUDDELL.

SIR,—The observations made by Dr. J. A. G. Horton and his colleagues in their article "Intra-arterial Transfusion" (*Journal*, December 12, 1953, p. 1294) are very instructive.

May I point out in this context in favour of intra-arterial transfusion that the whole principle may be looked upon as a second cardiac system, operating outside the body, feeding the whole arterial system with oxygenated blood directly under pressure when it is utterly impoverished, and thus filling adequately the coronaries and increasing the vis-a-tergo, improving the capillary stasis. In addition, the greatest advantage of this route is that it excludes the pulmonary circuit, which is definitely a retarding factor in the effectiveness of a transfusion through the venous route before the blood reaches the left heart. Thus, the more the patient is shocked, more rational it will be to choose the arterial route for transfusion for its immediate dramatic effect.—I am, etc.,

Braintree, Essex. R. CHAKRABARTY.

Polycythaemia Vera

SIR,—A patient may be said to have polycythaemia (rubra) if the red cell component of the blood of his whole body is decidedly in excess of the normal. But why should one call it polycythaemia *vera* (true polycythaemia) as if there were such a condition as false polycythaemia (pseudo-polycythaemia)? How can a polycythaemia be false, unless the patient or someone else has injected into his blood stream a substance imitating haemoglobin? Of course, the term "polycythaemia vera" was intended to mark a distinction from secondary polycythaemias, reactionary results of high altitudes, or malformations or diseases of the heart or lungs. But all such secondary polycythaemias are as real polycythaemias as so-called polycythaemia vera. Clearly, by the term "true polycythaemia" (polycythaemia vera) a condition of *primary* polycythaemia is meant—that is to say, polycythaemia of unknown origin, perhaps of neoplastic (or rather "neoplasic") nature, and not secondary to any known cause. In discussions on the subject I occasionally drew attention to this question, but mostly ignored it, in order not to turn an interesting discussion into one of nomenclature.

In nearly all genuine cases of primary polycythaemia there is an increase in the white cells at the very least in proportion to the increase in the red cells; this is a reason why the word "rubra" may be (as it usually is) omitted.—I am, etc.,

London, N.W.1. F. PARKES WEBER.

Succinylcholine Chloride for Casualty Anaesthesia

SIR,—I should like to comment on Dr. V. P. Wordsworth's first point in your issue of November 28 (p. 1219). The lower end of the oesophagus is controlled not by an intrinsic but by an extrinsic sphincter mechanism which is composed of three elements, first, the pinch cock action of the right crus of the diaphragm which forms the margins of the oesophageal hiatus, secondly, the sharp backward angulation of the lower end of the oesophagus caused by the contraction of the crura, and, thirdly, the acute angle of entry of the oesophagus into the stomach at the cardia. As the crura contain striated muscle Dr. D. C. Adamson's observation in your issue of October 31 (p. 993) that the cardiac sphincter relaxes during oesophagoscopy when succinylcholine is given would appear to be a correct one and is due to the property of the drug in question.—I am, etc.,

Hull. W. N. ROLLASON.

The Human Foot

SIR,—It was greatly encouraging to those whose approach to foot problems is not that of the surgeon to see two non-surgical papers on foot disabilities appear side by side in the *Journal* (October 3, pp. 745 and 749). The ensuing correspondence has shown how lively an interest is taken in this subject by readers whose thoughts are not bound by acceptance of clinical entities nor harnessed to therapeusis of conditions that should be preventable. But, Sir, having read the two papers and studied the material they offer with some care, I venture to ask how far have we been enlightened? Was this type of study in fact calculated to enlighten at this stage? Do the kind of questions both papers put to themselves—at enormous cost of time and labour—tell us anything that we did not know before?

It would be possible to discuss some of the evidence presented—I refer particularly to Dr. Doris Craigmile's paper (p. 749)—in slightly less serious vein. Reading the mass of assembled figures, I longed for a Mr. Schwartz on Sunday to spill them, big and small, into the air like soap-bubbles, juggle with them or let them fall in cascades of glistening fragility, and then return us to the real problems—to what is in fact a major social problem of this day. Not, however, being a Mr. Schwartz, may I put my queries in the form of a few direct questions?

Did we or did we not already know that foot deformities show an undesirable prevalence in early life? Do we or do we not agree that they take an undesirable toll of the comfort and energies, not to say looks, of the community of most Western populations? Are they not in fact costly? Do we or do we not believe that they are not congenital and, since they are eventually disabling, that it is our duty as a profession to prevent them, when our knowledge is great enough? Do we or do we not accept that certain deformities—differing only in degree, not in kind—are more common in adolescent girls and women than in males of the same age? Did we have to be informed that in old age, in a period of major tissue change and degeneration, symptoms mount, and are likely to mount, in both sexes (*pace* Dr. Craigmile's old ladies, who lose their bunions at 60) and assume new shapes and guises as a greater fraction of the anatomic complex—osseous, ligamentous, nerve, muscular and vascular tissues—is involved?

None of these things, I submit, requires laborious exposition, or analysis, at this stage. The relation between height, weight, and alterations in foot size (D. Hewitt *et al.*, p. 745) is far better

tackled, I would suggest, by insisting on the need for foot measurements every time new shoes are bought (at any age) than by demonstrating what is rational and manifest. Educate the public and the public will, in general, respond.

We, on the contrary, should get on with the problem of the proper protection of the child from early youth into the more mature periods of life, in which new and un-understood factors are unlikely to irrupt unbidden, but in which old stresses will begin to show cumulative effects until eventually, in old age, the declension of the entire being causes a calling-in of mortgages, an auditing of *all* the outstanding accounts of preceding years, that may transmute the clinical characters of what started as a local traumatic lesion. In general, foot deformities are traumatic lesions. Let us deal with the trauma.

If the two studies have provided no major enlightenment, do any points emerge on which further questions arise? I found the following: (*a*) Some negative evidence in the matter of heel heights and disability—a point still fully open to discussion. (*b*) Some negative evidence on the inadmissibility of varus metatarsus I as a factor contributing to deformity, the chief point being its apparent tendency to "recede," in both sexes, between the ages of 5 and 15 years. Was this information confirmed by *x*-ray examination? (*c*) A failure to observe annual, as opposed to month by month, fluctuations of growth in the feet of the two sexes that might have contributed positive evidence of the effects of specific periods of growth: in particular, a failure to check the effects, if any, of the peculiar spurt of growth manifested by children's feet in the sixth year of life.[1] (*d*) Some negative evidence, worth clarifying further, on the effects of specific periods of growth on foot deformity—i.e., the considerable increase in cramping of the toes observed by Dr. Craigmile in girls coincidentally with the "third springing-up period" (11–12 years)[1] which comes two years earlier in girls than in boys. (*e*) A considerably higher rate of valgus ankles in boys than in girls, declining steadily in boys during the school-age period. Could this derive from the later ossification of the secondary epiphyses of the os calcis in boys—at 8 years as opposed to 6 in girls? Does this symptom, very prevalent in both sexes in pre-school life, hinge partly on the presence or absence of the tubercles, of which the posterior medial is the largest, that develop on the lower surface of the os calcis, enabling it to maintain its even keel? How far is the whole symptom of valgus ankles in early youth linked, *inter alia*, with the practice of having a flat, *upper* heel surface in the shoe, which does not correspond with the inclined plane of the lower surface of the os calcis, minus its tubercles? (*f*) Some very interesting observations on pes cavus in males at all ages. Has this symptom (I use the word advisedly) ever been related to nervous tensions? Has anyone ever examined statistically the frequency of pes cavus in mental patients of both sexes?

Some bubbles after all sustained their flight! But I revert to my thesis that the work of the future lies with the feet of the children, and with a study of physiology rather than pathology.—I am, etc.,

London, W.1. MARGARET EMSLIE.

REFERENCE

[1] Harris, H. A. (1947). In *Child Health and Development*, edited by R. W. B. Ellis. Churchill, London.

SIR,—For many years I have been conducting experiments on wear and shrinkage of men's socks, as it had become apparent that many minor disorders of the forefoot were directly attributable to the compression of the toes by hosiery. Among the types tested were the oily woollen fishing socks which are readily available in towns on the West Coast of Scotland, and, although these socks were satisfactory from the aspect of wear and minimum shrinkage, they are rough in texture and quite unsuitable for town wear, although they are remarkably satisfactory for long-distance driving provided there is adequate room in the shoes to accommodate their bulk.

The most unsatisfactory types under test were all-wool hand-knitted socks, which show quite remarkable shrinkages (up to 30%) although they are washed with great care, while the manufactured socks stamped "guaranteed unshrinkable" give some loss of length and girth. Wool and rayon, and wool and nylon reinforced, socks had little or no advantage over the pure wool or wool and cotton mixtures; cotton socks rapidly became harsh and uncomfortable in wear.

On May 13, 1952, I purchased three pairs of 100% spun nylon socks, and one pair was retained as a control while the other two pairs were worn on alternate days until the end of June, 1953. Each sock was worn and washed 200 times and each was subjected at various times to soaking or boiling in 20% "lysol," 5% "dettol," as well as soaking and boiling in almost every available proprietary washing powder and detergent. The texture of the material has remained very good for 18 months; there has been no breakdown in texture, no holes have appeared, and the length and girth of the test socks still remain identical with the unwashed control socks.

I was surprised to find that the socks were as cool as the same weight of cashmere sock in the summer, and at least as warm as the same weight of woollen socks in the winter, and I was not conscious of cold feet even while driving an unheated 1939-model car. A very notable feature was the quite extraordinary amount of dust or grime in the washing water at each washing. It appears that dirt is much more easily removed from nylon material than from wool, and I feel that these socks would be useful for patients suffering from hyperidrosis and bromidrosis in particular, and from other skin conditions where cleanliness of the skin of the feet is essential. Several of the commercial washing powders will remove ointment bases from the nylon.

Subsequent tests have shown that daily washing of the socks gives the most satisfactory results, as three, four, or five intervals produce a temporary hardening of the foot of the sock, something like the hardness found in cotton material. As I give quite a number of talks on "foot care" to women's institutes each year I have been a little amused to discover that none of the members (among whom there are many ardent knitters) has been able to identify the spun nylon socks, and these women, who are usually knowledgeable about materials, were surprised to find that the socks were not pure wool.—I am, etc.,

London, S.W.3. C. E. KEMP.

Hypothermia

SIR,—Your leading article on hypothermia (*Journal*, December 5, p. 1256) interested me considerably, for, as I pointed out some years ago,[1] and probably many others have realized it too, there are many points in common between the action of cold and morphine. Both reduce the body temperature, both depress respiration, and, especially, both reduce the demands of the tissues for oxygen—that is, slow metabolism. Morphine, of course, has also marked effects on the central nervous system, but these are, on the whole, entirely beneficial in anaesthesia. It would seem right therefore to point out that in giving morphine before anaesthesia we are, in some degree, actually achieving some of the advantages claimed for hypothermia. The problem is, How far can we go and what can be done to prevent the obvious possible dangers of increasing the dose of morphine?

In the article quoted I mentioned the case of a missionary in India who had tried to put a woman in the bush out of her misery by giving her an overdose of morphine, only to be greeted by her some years later as the man who had saved her life. I recall, too, a girl who was apparently dying of general peritonitis after an operation (this was in 1915) to whom the house-surgeon, confusing liquor morph. with the injectio morph., gave ten times the dose he had intended. He spent a most uncomfortable week-end while the girl slept solidly, but on the Monday his chief was surprised to find her so much better and she eventually recovered. No doubt many other stories of the life-saving power of morphine might be cited, and no less of unexpected fatalities.

If morphine is to be used for these often unconsidered effects I think we must realize certain things. First of all, its benefit is often mainly due to the fact that it diminishes the tissue demands for oxygen, and if after giving it we persist in trying to maintain the body temperature by hot-water bottles, etc., we are inevitably increasing these demands and so undoing the benefit we may otherwise obtain. It is, indeed, questionable how right we are physiologically in trying to keep up the temperature of a patient during operation if he has had morphine previously. It might be safer to let the temperature drop a little, for the traditional prevention of shock after an anaesthetic by keeping the patient warm was established, as I know, before premedication was at all common. Furthermore, later studies—long after my day—of

electrolyte balance, etc., after operation have shown what a baneful effect fluid loss has; and maybe our present technique is unconsciously increasing this.

The next thing is that morphine undoubtedly depresses respiration. Now Barcroft's work,[2 3] to which I referred in a letter recently (*Journal*, August 29, p. 510), showed that in the foetus (and the same probably holds throughout life) asphyxia progressively alters the source of the respiratory rhythm from the respiratory centre itself to lower and lower portions of the C.N.S., and that these respond, not to oxygen lack, but to external or internal stimuli. He pointed out that one of these stimuli is certainly muscle tone, and with the increasing use of muscle relaxants it is clear that this source of respiratory stimulus is diminished or abolished. It is therefore of the utmost importance that any patient who has had morphine should be ensured of an abundant supply of oxygen if normal respiration is to be maintained.

The last point I make is that we have now at hand many agents which can, in case of need, counteract some of the dangers of morphine therapy. As you pointed out in an annotation (*Journal*, August 8, p. 329), the newly introduced N-allyl *nor*morphine has in some unknown way the power of rapidly counteracting the depressive effect of morphine on the respiratory centre. Chilling is not, of itself, a cause of infection, for infecting organisms all multiply very much faster at higher temperatures, but penicillin (and possibly other antibiotics) should prevent chest complications, for the shallow respiration of morphine narcosis is not, *per se*, a cause of congestion or atelectasis; in fact cardiac action, and so the circulation, is probably relatively improved rather than diminished by morphine.

This last statement is, I think, substantiated by the life-saving properties of morphine in cases of coronary thrombosis—not that I am here belittling in any way the effect of the anticoagulants. The question does arise, however, whether when we have given morphine to such cases we do the best for them by keeping them warm, or whether they would not really have a better chance of recovery if we allowed their temperatures to fall to, say, 96° or even 95° F. (35.6° or 35° C.), as in fact it naturally does unless we take measures to prevent it. Admittedly all these points are hypothetical, and perhaps highly controversial, but I think they do arise and that modern treatment might possibly be improved if they were answered, or at least were present in the minds of those who undertake to teach it.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

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2 *British Medical Journal*, 1939, 2, 986.
3 *Researches on Pre-natal Life*, 1946. Blackwell, Oxford.

Infected Urine

SIR,—The article by Mr. Cuthbert Dukes (*Journal*, December 5, p. 1262) on infected urine in the series "Clinical Pathology in General Practice" has been greatly appreciated, but it is felt that it is concerned more with the examination of urine in the laboratory rather than in the surgery or even the clinical sideroom. It is regretted that Mr. Dukes did not deal more fully with the examination of urine for pus. Usually this is the first, and perhaps the only, test that needs to be done by the general practitioner when faced with a suspected case of renal tract infection. For this purpose, as Mr. Dukes mentions, microscopy is essential, and it is agreed that "the simplest and quickest" way of doing this is by examining a measured quantity of urine, using a counting chamber (an ordinary blood counting chamber may be used if a Fuchs–Rosenthal is not available). Not only is the counting chamber method to be recommended because it is easy to do, but it is also much more useful than the microscopic field counts' method, for it avoids its ambiguity and detects small but significant quantities of pus that otherwise would be missed. The interpretation of microscope field counts of pus cells can be very confusing, as the range of normal excretion cannot be determined precisely since the method is so inaccurate and the quantities of urine examined are variable. On the other hand, Mr. Dukes himself has ascertained the limits of normal excretion of pus cells measured in a counting chamber for uncentrifuged urines from adults,[1] and I wish he had emphasized the value of this method.

Recently observations have also been made on children of all ages[2] using the counting chamber method. Briefly, it appears that in males and catheter specimens from females urines usually contain less than 50 cells per c.mm., between 50 and 100 cells is suspicious, and over 100 abnormal. In females contamination may occur, but over 500 cells per c.mm. indicates probable infection.

Finally, Mr. Dukes has not mentioned the need for repeated urine examination in a suspected case of renal tract infection. Both pyuria and bacilluria may be intermittent. The diagnosis of renal tract infection cannot be ruled out on the evidence of a single specimen of urine which is normal.—I am, etc.,

Durham. J. M. STANSFELD.

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1 *Proc. roy. Soc. Med.*, 1928, 21, 1179.
2 Stansfeld, J. M., and Webb, J. K. G. (1953). *Arch. Dis. Childh.*, 28, 386.

Unwrapping the "Journal"

SIR,—May I recommend to the attention of your correspondents the following method of resection of the wrapper of the *British Medical Journal*?

An ordinary dinner knife is required. With its aid the free ends of the leaves of the *Journal* are located at one end of the package, and the knife is gently inserted so that it lies between the leaves, with its sharp edge pressing against the wrapper. The knife is then pushed, with a saw-like motion, to the other end of the package, cutting the wrapper as it moves. By this method the *Journal* can be shelled out, like a sebaceous cyst, with minimal laceration both of the operator and of the pages. We in this college would not recommend the attempt without the use of what Dr. Lyndhurst Duke (*Journal*, December 12, p. 1326) describes as a special implement, any more than we would recommend an appendicectomy performed with the bare hands.—I am, etc.,

London Hospital Medical College. STEPHEN BUTTERWORTH.

A Cosmetic Amputation

SIR,—When those who are amongst the acknowledged leaders of our profession express opinions, these opinions are likely to have a wide hearing. It is therefore unfortunate that opinions which may be controversial should be expressed as *ex cathedra*, as they may then be accorded full and indeed overriding authority. It is particularly unfortunate when the vexed questions which arise in assessment of disability for the purposes of insurance are made the subject of opinions expressed in this way. For these reasons I consider Sir Heneage Ogilvie's letter (*Journal*, December 12, 1953, p. 1322) to be regrettable.

My experience of amputation of the index finger or of the little finger is that many patients are more comfortable and are less functionally disabled if the distal part of the metacarpal is removed. It is not my experience that the movement of the adjoining finger is limited if the amputation is performed in this manner, nor that the occurrence of painful neuromata is more common if the associated metacarpal is removed; indeed, I think it is less so. It is a fact that, if the metacarpal is removed, the scar of amputation can be placed dorsally where it is free from the impacts which fall on the palm or upon the terminal projecting stump which must result from disarticulation of the finger without removal of the metacarpal. The only patients who are adversely affected by lack of breadth of the palm are those engaged in the gripping of heavy objects with large handles such as picks, shovels or heavy hammers, and not all of them are. Those who are working with machinery commonly find the metacarpal stump a considerable nuisance, and indeed often return asking to have it trimmed.

I propose to continue to remove the index finger with the removal of the associated distal part of the metacarpal in most patients requiring this amputation.—I am, etc.,

Edinburgh. IAN LAWSON DICK.

Chronic Gastric Ulcer

SIR,—Your statement in your leading article (*Journal*, October 17, p. 871) that "in ordinary clinical practice the combination of careful radiology, aided when necessary by gastroscopy, can safely distinguish between them [benign gastric ulcer and early, ulcerating gastric cancer]" is a most remarkable one, and seems to me to require examination and comment.

The phrase "in ordinary clinical practice" is not clear to me. Do you mean by "ordinary" a practice in which the bulk of the patients are just average, run-of-the-mill citizens—perhaps with their medical fees prepaid through taxes—or a general practice, as distinct from one limited to gastro-enteric diseases? The inference that you are referring to some sort of *milieu* in which no very great degree of exactness of diagnosis need be aimed at seems virtually inescapable to me. I trust I have not understood you correctly.

I do not understand, certainly, your implication that the comparative unlikelihood of malignant degeneration in a benign gastric ulcer (which is admitted by most workers, I am sure) contravenes in any way the belief of "many workers in the U.S.A." that "a gastric ulcer carries a 10% chance of malignancy." The word "But," initiating this sentence, seems quite gratuitous. The only thing wrong with your statement about the American workers is that the figure given is too low. Lampert, Waugh, and Dockerty[1] found 13% of 550 radiologically and clinically benign gastric ulcers to be malignant histologically. Allen[2] found 14% to be malignant under the microscope. Smith and Jordan[3] at the Lahey Clinic found 21% of apparently benign gastric ulcers were actually early gastric cancer. Banks and Zetzel[4] found that 8 of 48 cases of chronic and apparently benign gastric ulcer died of carcinoma.

I know of no radiologist, nor any gastroscopist, who believes he can say with assurance of any ulcerating gastric lesion that it is definitely not a carcinoma. As long as any such statement has to be prefaced with "probably," the decision should be left to the pathologist—quite apart from the fact that about one out of four victims of truly benign gastric ulcer receives any lasting benefit from medical treatment.—I am, etc.,

Hawaii. HARRY L. ARNOLD, jun.

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1 *Surg. Gynec. Obstet.*, 1950, **91**, 673.
2 *Surgery*, 1945, **17**, 750.
3 *Gastroenterology*, 1948, **11**, 575.
4 *New Engl. J. Med.*, 1953, **248**, 1008.

*** We meant by the words "in ordinary clinical practice" to indicate general or special practice in places where diagnostic facilities are available in hospital or clinic.—ED., *B.M.J.*

Hexamethonium in Acute Pancreatitis

SIR,—In view of the interest aroused in the article by Mr. Russell Davis, Mr. F. T. Moore, and Mr. D. Wynn-Williams (*Journal*, December 5, p. 1251), it may be valuable to record our experiences in this subject. In 1949 we concluded that if hexamethonium would abolish the secretion of hydrochloric acid and inhibit gastric motility for three or four hours it would also serve to diminish or even abolish the production of secretin by the duodenal mucosa. If this proved to be the case, it should then be of value in pancreatitis purely from the point of view of resting the gland. With this in mind, we tried to assess its activity in normal individuals. A Rehfuss tube was passed into the second part of the duodenum under the *x*-ray screen, 100 ml. of 50% glucose was given by mouth, and suction applied for 4 hours. The following day the experiment was repeated with 100 mg. of hexamethonium given intramuscularly at the same time. The pancreatic juice was measured and its tryptic activity and *p*H were assessed by Dr. MacGowan. The amount of trypsin was considerably reduced in five cases and was unchanged in one. The changes in *p*H were not significant, but in all except one case the volume of the pancreatic juice secreted during the four hours was markedly diminished. This crude experiment suggested that hexamethonium exerted an effect on the pancreas, either by the suppression of secretin or possibly by its autonomic ganglionic blocking activity on the pancreas itself.

Between October, 1949, and February, 1952, with the help of our colleagues in the clinical area, we were able to observe and treat 24 cases of acute pancreatitis. (We took as our criteria a serum amylase above 250 units, associated with severe upper abdominal pain of fairly sudden onset, with vomiting. Actually many cases had a serum amylase above a thousand.) Eighteen of the 24 cases were treated with hexamethonium. In all but five cases there was relief of pain, relief of vomiting, and steady clinical improvement under a dose of 25 mg. four-hourly. Three cases died; two of them after 24 hours with an acute haemorrhagic pancreatitis. The other one died on the third day from coronary thrombosis. Hexamethonium had given complete symptomatic relief. In three cases there was no apparent relief of pain but they nevertheless recovered. One case had no relief from his pain, but there was immediate benefit from intramuscular methantheline ("banthine"). In four cases the blood pressure was so low on admission that it was not deemed advisable to give hexamethonium. Three of these cases recovered.

It was apparent from this that, although hexamethonium gave relief from pain, its side-effects, and especially that of further lowering the blood pressure in an already grave condition, did not make it an ideal drug in this disease. We were of the opinion that methantheline or propantheline bromide ("probanthine"), or even atropine, pushed to its limits, give equal relief without the dangerous lowering of blood pressure. We therefore abandoned its use as a routine measure.

It seems to us that the response to hexamethonium in pancreatitis cannot be held to indicate that thrombosis, embolism, or infarction is a primary aetiological factor. We cannot believe that a further lowering of blood pressure of 10 to 20 mm. Hg is likely to benefit thrombosis or infarction. It is more likely that improvement is due to diminished formation of secretin.

Finally, if laparotomy for this condition is recommended in order to assess the degree of destruction of the gland, then the mortality will steadily rise. In our view, the correct treatment according to our present knowledge (or ignorance) of the aetiology consists mainly in very careful gastric aspiration to prevent acid passing into the duodenum, together with a full dose of methantheline or atropine, and supportive therapy. Hexamethonium should only be given initially where the blood pressure is not seriously lowered and continued only where dangerous hypopiesis does not develop. We cannot believe that laparotomy could affect the outcome otherwise than adversely.—We are, etc.,

W. M. CAPPER.
Bristol. FRANK I. TOVEY.

Appendix in the Hernial Sac

SIR,—In view of the recent correspondence on inflamed appendices in hernial sacs, it may be of interest to record a case in an obturator hernia which came under my care in Italy during the war.

The patient was in the W.R.N.S., in the early 20s, and complained of moderately severe right-sided lower abdominal pain. On vaginal examination a hard, tender mass could be felt over the right obturator foramen. In view of this, some displacement of the uterus, and a positive Howship-Romberg sign, a provisional diagnosis of obturator hernia was made. At operation the fimbriated end of the right Fallopian tube and about 1 in. (2.5 cm.) of the appendix were found to be adherent in the sac and inflamed, the right ovary lying over and blocking the foramen. The tube and appendix were reduced and separated and the appendix removed, but not the Fallopian tube, and the sac repaired. Convalescence was uninterrupted.

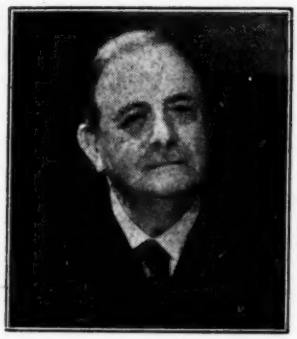
I reported this case to the North of England Obstetrical and Gynaecological Society, and fuller notes can be found in the proceedings for 1946.—I am, etc.,

Manchester. DUDLEY RACKER.

Obituary

THOMAS COCHRANE, M.B., C.M.

Dr. Thomas Cochrane, who died suddenly at Pinner, Middlesex, on December 7, 1953, at the age of 87, graduated in medicine at Glasgow University in 1896. He then went for a short time to do pioneer medical mission work in Mongolia, and in 1901 he was asked to go to Peking to reorganize medical work in that city, where everything had been destroyed during the Boxer troubles of 1900. He was soon asked to fill important posts. For example, he was known to be interested in bacteriological and public health work, and during an outbreak of cholera he inaugurated and conducted the first official public health campaign in China for the Chinese Government, with the support of Prince Su and Sir Robert Hart. He was appointed medical officer to the Imperial Maritime Customs and adviser to the Chinese Government. He was acting medical officer for some time to the British Legation at Peking and did medical work in most of the legations in the capital besides attending the highest officials in the empire and the court of Peking.



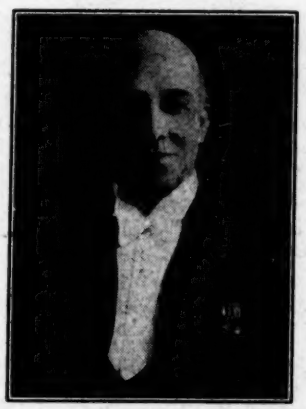
But Cochrane's greatest contribution to China was in connexion with education. He helped to form and was for a time president of the North China Educational Union, out of which grew the present large university scheme in Peking. He founded and was the first principal of the Peking Union Medical College, which in his hands became the most efficient medical college in China and was taken as the model for government institutions. This college has now become one of the great medical colleges of the world and has made contributions of world-wide value—for example, in the discovery of ephedrine and in other directions. He was appointed one of the trustees of this institution on the Rockefeller Board in New York. He was the first foreigner in China to petition the throne in the interests of scientific medical education, and he received the first and only gift ever made by the throne to a foreigner for educational purposes. The large sum of money he received from the Empress Dowager was followed by a grant of land from the Emperor. A committee was formed, composed of a grand councillor, the president of the Board of Finance, and Sir Ernest Satow, the British Minister: the Chinese members of this committee intimated to all the provincial governors the contribution made by the Empress Dowager, and her example was quickly followed. When the college was built a high commissioner was appointed by the throne to declare it open, which he did in the presence of the most brilliant international assembly that China had ever seen, including princes, dukes, grand councillors, presidents of government departments, and representatives of all the foreign powers. The board of education gave the college the unique privilege of recognition, and the government made annual grants towards the current expenses of the institution. Dr. Cochrane made other contributions to China through his literary activities, which included *Lectures on Osteology* (in Chinese), a translation of Heath's *Practical Anatomy* into Chinese, *A Survey of China*, and *A Survey of Medical Education in China*.

In 1915 Dr. Cochrane returned to England, where his influence and statesmanship in missionary matters were at once in evidence. He and the late Mr. S. J. W. Clark, influenced very largely by the writings of the Rev. Roland Allan, founded the Survey Application Trust, the object of which was to encourage indigenous principles in missionary planning and to emphasize priorities. The trust sponsored the World Dominion movement which has had a profound influence in missionary strategy. He was editor of *World Dominion* (an international review of Christian progress) since its inception in 1923. In 1931 he founded the movement of World Evangelists, of which he was president. He was a recognized authority on religious, social, educational, and medical mission situations throughout the world and the author of many published surveys.

Dr. Cochrane married in 1896, and his wife shared all his early adventures before the Boxer rising in China. His first wife died in 1930; he married again in 1935 and is survived by his widow and three sons, all of whom are in the medical profession.

CYRIL HORSFORD, M.D., F.R.C.S.

Mr. Cyril Horsford, one of the older generation of laryngologists—probably even better known among singers and actors than in his own profession—died in London after a short illness on December 16, 1953, at the age of 77. It was as a consultant particularly helpful in the ailments of the throat and problems of the voice of singers and actors that Cyril Horsford made his reputation, and at the height of his career he was one of the best-known laryngologists in London. He was himself an accomplished musician, and during the opera seasons at Covent Garden his house was a rendezvous of foreign operatic stars, whose carefree and uninhibited singing in Horsford's friendly salon was wont to enliven the early hours of the morning in Harley Street. Many famous singers have expressed their gratitude in no uncertain terms for Horsford's timely help.



[Hay Wrightson, London

Born at St. Kitts, in the West Indies, on January 25, 1876, Cyril Arthur Bennett Horsford was the son of the Hon. S. L. Horsford and was educated at Bedford Modern School and at Edinburgh University. He graduated M.B., Ch.B. in 1898 and proceeded to the M.D., with honours, in 1902, becoming a Fellow of the Royal College of Surgeons of England in the following year. He was appointed a clinical assistant at the Throat Hospital, Golden Square, in 1902, and from 1905 to 1913 he was registrar at the Central London Throat Hospital. Subsequently he received appointments as honorary laryngologist to the Princess Beatrice Hospital, Kensington, and as surgeon in charge of the

throat and ear department of the St. Pancras Dispensary. During the war of 1914–18 he served for a time in the R.A.M.C. as an aural specialist with the rank of captain. For many years he was honorary laryngologist to the Royal College of Music, the Royal Choral Society, and the Royal Society of Musicians, and was a popular lecturer to non-medical audiences on such subjects as the anatomy and physiology of the larynx.

Cyril Horsford's contributions to medical literature were comparatively few, but they were all helpful and practical. In discussions at meetings of the section of laryngology of the Royal Society of Medicine he was an occasional but always pungent contributor; and he was a loyal and regular attender at the dinners of the Edinburgh University Club in London, of which he was one of the oldest members. He married Miss Edith Louise Sayers, adopted daughter of the late Miss Lascelles-Jones, and had a son and a daughter, with whom he led a most happy and devoted family life.—R. S. S.

ADAM BARR, M.B., F.R.F.P.S., F.R.C.O.G.

Dr. Adam Barr, senior obstetrician and gynaecologist at Stobhill Hospital, Glasgow, died suddenly on December 11, 1953, while on his way home from hospital. He was 60 years of age.

Adam Barr was born on May 29, 1893, at Rutherglen, a royal burgh on the outskirts of Glasgow, and there he spent the early years of his life. He graduated M.B., Ch.B. at Glasgow University in 1921, his medical course having been interrupted by a period of service as a combatant in the first world war. After graduation he held several house appointments and then spent five years in general practice. But he had always been much interested in obstetrics, and as soon as the opportunity offered joined the staff of the Royal Maternity and Women's Hospital and the Royal Samaritan Hospital in Glasgow. In 1929 he was given charge of the obstetrical and gynaecological units of the Eastern District, Western District, and Stobhill Hospitals, and, while holding these appointments, acted for a time as professor of midwifery in the Anderson College of Medicine. He relinquished this post to become senior assistant to Professor S. J. Cameron at the university and at the Western Infirmary. He was elected F.R.F.P.S. in 1926 and two years later he took the diploma of L.M. of the Royal College of Physicians of Ireland. In 1940 he became a Fellow—he was a founder member—of the Royal College of Obstetricians and Gynaecologists.

More recently he retired from private practice and from his other hospital appointments and devoted himself entirely to his work as senior obstetrician and gynaecologist at Stobhill Hospital. Under his supervision the obstetrical and gynaecological unit there developed into a department of over 200 beds. The university, recognizing its importance, appointed Dr. Barr an honorary lecturer in clinical obstetrics and gynaecology and arranged that he should undertake the teaching of a considerable number of the university students. He also acted as examiner to the university, to the Central Midwives Board, and to other institutions, including the Royal Faculty of Physicians and Surgeons of Glasgow.

Dr. Barr excelled as a clinician, a teacher, and a consultant. As a teacher, he never forgot that the majority of his students would enter general practice, and he made it his business to fit them for their task. His own early experience and his gift of stating the essentials in plain terms enabled him to do this with outstanding success. For the same reason no postgraduate course was complete without his lecture on midwifery in general practice. He acquired a very large private practice, which with his hospital work kept him so busy that he had little time for research, even if his interests had leaned in that direction. But his main concern was with the purely practical aspects of his specialty, and his published work deals exclusively with practical matters. Perhaps his most outstanding contribution was the development (in conjunction with Dr. Andrew Tindal) of the Barr–Tindal apparatus for the self-administration of gas and oxygen. Other pieces of work included an investigation into the value of serum in the treatment of puerperal sepsis, and the use of "prontosil" in cases of renal infection.

Outside medicine his main pleasures were a love of the countryside and a keen interest in the Church. He was a devout churchman and took an active share in the services and in the social work of the congregation to which he was attached. He was particularly fond of the old Scottish psalm tunes, and when unable through pressure of work to attend a service he used to play over to himself the records of the old psalm tunes as sung by the Glasgow Orpheus Choir. Dr. Barr is survived by his wife, who is also a doctor, and by his only child (a daughter), who is a second-year medical student; to them, and to his other relatives, we extend our deep sympathy.—J. H.

WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G.

C. R. M. writes: As a house-surgeon—many years ago—of the late Wilfred Shaw, whose obituary was printed in the *Journal* of December 19, 1953 (p. 1380), I should like to pay a humble tribute to a great man. Although he will always be remembered for his work in science—especially on ovarian tumours—I shall always think of him as a superb clinician, operator, and teacher. He must occasionally, like all of us, have made clinical mistakes, and yet I cannot recollect an occasion when this occurred. The search for truth was the objective from which he never deviated. Ready at all times to consider the opinions of others, he was equally stubborn in defending his own unorthodox views, if he was sure that he was right. His genius for sifting the mass of material in the modern medical press was remarkable, and a day or two spent with him in the operating theatre, out-patients, or on a ward round were worth any postgraduate course or conference.

To his old students, or for that matter any visitor, he was an inspiration and ever ready to help, advise—or listen. I was privileged to see the proofs of his *Operative Gynaecology*, fortunately completed. This magnum opus, not yet published, will undoubtedly be the brightest star among his other well-known publications. The loss of this remarkable man at such an early age is indeed a severe one to British obstetrics and gynaecology.

The Services

Brigadier A. Sachs, C.B.E., Q.H.P., late R.A.M.C., has been appointed D.D.M.S., and has been granted the temporary rank of Major-General.

Captains R. P. Hickey and D. R. Patchett, R.A.M.C., have been awarded the Military Cross in recognition of gallant and distinguished services in Korea.

Surgeon Captain A. A. Pomfret, O.B.E., R.N., has been appointed Honorary Surgeon to the Queen in succession to Surgeon Captain M. Brown, R.N., who has been placed on the Retired List.

Medico-Legal

BELL'S PALSY IN DRAUGHTY OFFICE

A South-western Electricity Board temporary clerk, Mr. N. L. Andrews, aged 53, of Minehead, Somerset, unsuccessfully brought an action for damages against the Board before Mr. Justice Parker at Devon Assizes recently on the grounds that when employed in the Board's office between December, 1951, and March, 1952, he had to sit in draughts which caused him to suffer from Bell's palsy, with a result that he was now prevented from doing any sustained work. His case was that for the rest of his life he would suffer a considerable degree of disability, and the disease was one which could be caused by exposure to draughts.

Since Mr. Andrews had contracted the disease the Board had fitted draught-excluding devices to the windows and doors of the premises.

Dr. P. B. Stirling Cooper, of Minehead, said he believed that Mr. Andrews's complaint was caused by a draught on the side of his face.

Dr. T. Rowland Hill, consultant in neurology, said the form of palsy from which Mr. Andrews suffered was nearly always caused by a draught striking the face. He thought Mr. Andrews was truthful when he said that he could not work for any longer than half an hour without getting a splitting headache. There had been a nervous reaction in Mr. Andrews, although in about 18 months the patient might be able to do a full day's work again.

The defendants contended that, if the plaintiff was right, even people who had got influenza might be taking out writs against the transport authorities for allowing draughts in trains and buses. An employer was bound to take reasonable precautions for the safety of his employees, but precautions against draughts fell into the category of welfare and not safety. It was not certain that Bell's palsy was caused by draughts. From clinical experience it was thought that was probable, but it had not been established.

Judgment

Giving judgment, Mr. Justice Parker said that on March 30, 1952, Mr. Andrews woke up with his jaw distorted, his left eye closed, and the whole of the left side of his face paralysed. The complaint was correctly diagnosed as Bell's palsy.

It was the plaintiff's case that the disease was caused by the negligence of his employers. A plan showed the office in which Mr. Andrews worked for the Board to be a passage room. Witnesses had said that the office was very draughty and cold with badly fitting doors, and people who walked through left the doors open. But there had been a good deal of exaggeration in the evidence given on the part of the plaintiff, and he was satisfied that the office was no more draughty than any other office, subject of course to its being a passage room.

The latest theory was that certain people were predisposed to Bell's palsy. On the balance of probabilities he was satisfied that in the Board's office the conditions did precipitate that disease in a man already predisposed towards it in the sense that he already had a virus infection of a nerve. There was no question of the employers' having the slightest knowledge or suspicion that the plaintiff was so predisposed to that disease. Eliminating that, one asked oneself what steps a reasonable and prudent employer should take in regard to his office staff in conditions such as those in that case. Conditions in the Board's office were quite comparable with those existing in other offices and were not such as the employers ought reasonably to have foreseen injury to health, although they might well recognize that there was discomfort, as opposed to danger to health. The defendants in that case had not been guilty of any breach of duty and the claim therefore failed.

Universities and Colleges

UNIVERSITY OF OXFORD

In a Congregation held on October 31 the following medical degrees were conferred:

D.M.—R. G. White, E. O. Field, E. C. Hoff.

The Board of the Faculty of Medicine has awarded medical scholarships to Roland David Stedeford (Worcester College) and Ortwin Answald Alwin Bock (University of Pretoria).

UNIVERSITY OF CAMBRIDGE

In Congregation on November 14 the degree of M.A. was conferred on F. W. Campbell, Ph.D., M.B., Ch.B., University Lecturer in the Department of Physiology, and the degrees of M.B., B.Chir. on R. J. Hutchinson (by proxy).

The following degrees were conferred on October 31:

M.D.—D. H. M. Woollam, T. M. Robinson, R. B. Welbourn.

M.A.—C. W. McE. Pratt, M.B., Ch.B., University Demonstrator in Anatomy.

M.B., B.CHIR.—Mrs. Stella M. E. Ambache (by proxy).

UNIVERSITY OF ABERDEEN

The following medical degrees were conferred on October 28:

CH.M.—G. E. Mavor.

M.B., CH.B.—Frances Allan, J. G. Barnett, G. R. Buchan, Vera C. Coutts, B. B. Dale, N. L. Edmond, J. D. Garden, W. Geddes, J. D. Johnston, D. Macintosh, J. McNab, C. O. Macrae, A. N. Milne, V. J. Murphy, G. G. Rennie, T. F. Rennie, N. F. Stewart, J. V. Watt, Isobel M. Wood.

UNIVERSITY OF LONDON

The Court of the University has re-elected Sir Archibald Gray as deputy chairman, and Dr. C. F. Harris has been elected chairman of the Academic Council.

Dr. P. W. Rowland has been reappointed representative of the University on the governing body of the Colchester Royal Grammar School.

Mr. J. H. Doggart has been recognized as a teacher of ophthalmology of the University at the Institute of Ophthalmology.

The Laura de Saliceto Studentship has been awarded to Dr. H. J. G. Bloom for a period of two years in the first instance from October, 1953; the A. H. Bygott Scholarship, tenable for one year, to Dr. T. A. Plumley; a University Studentship in Anatomy to A. W. Rogers (London Hospital Medical College); and a University Studentship in Physiology to J. J. Misiewicz (St. Bartholomew's Hospital Medical College).

The title of Reader in Entomology, as applied to Hygiene, in the University has been conferred on J. R. Busvine, Ph.D., D.Sc., in respect of the post held by him at the London School of Hygiene and Tropical Medicine.

The following degrees were awarded by the Vice-Chancellor on behalf of the Senate on September 30:

M.D. (INTERNAL).—Helen Ingleby.

M.S. (INTERNAL).—F. B. Cockett.

UNIVERSITY OF WALES

The following candidates at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

TUBERCULOUS DISEASES DIPLOMA.—T. B. Master, J. Morgan, C. Michie, B. Sinha.

UNIVERSITY OF LEEDS

Dr. D. G. F. Harriman has been appointed Lecturer in Neuropathology in the Department of Pathology.

UNIVERSITY OF SHEFFIELD

The following appointments are announced: Dr. Alison Chapman, Whole-time Assistant Medical Officer to the Student Health Service; Dr. T. Smith, Part-time Lecturer and Clinical Teacher in Obstetrics and Gynaecology; Dr. D. H. Blakey, Part-time Honorary Tutor in Obstetrics and Gynaecology; Dr. R. S. Weetch, Part-time Honorary Lecturer in Therapeutics.

Dr. M. G. Philpott has resigned his appointment as Tutor in Child Health.

The John Stokes Medical Research Fellowship has been awarded to Mr. R. Whittam.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of the College held on November 3, with the President, Dr. W. A. Alexander, in the chair, the following were elected Fellows of the College: R. V. Rajam, Sir Peter MacCallum, R. Morrison, Jean M. Grant, G. H. Armitage, S. Chaudhuri, I. R. C. Batchelor, A. G. S. Hill, E. M. Heller, R. C. L. Batchelor, J. O. Forfar, W. A. Karunaratne, J. H. Wright, G. M. Fyfe.

The following were elected Members of the College: T. K. Maclachlan, E. Hacker, S. S. Maitra, L. D. Walters, B. A. Bradlow, E. Taube, V. M. Hercus, W. Cooper, R. L. Walker, H. Watson, J. O. Taubman, M. G. Pradhan, F. W. Tadros, J. D. Andrew, S. A. Biggart, G. R. Tudhope, D. W. Dawson, H. M. Macleod, N. K. Sarkar, S. Sachdev, J. D. Haldane, A. K. Dutta, A. P. Kumbhani, T. T. S. Ingram, B. Zilberg, J. Blake.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on October 21, with Professor Walter Mercer, President, in the chair, the following were admitted Fellows of the College after having passed the requisite examinations: F. O. Adewole, M. Ahmad, D. Crichton, A. B. McL. Currie, E. Davidowitz, K. R. Daymond, L. P. Eaton, F. Elahi, J. M. Foreman, T. E. Haddad, S. A. Hamid, J. M. Hastings, H. Kee, H. Klein, P. Lakshmipathy, W. Markkanen, M. K. Mehra, N. D. Motashaw, H. H. Neifeld, K. M. Said, G. P. Srivastava, N. L. Stokoe, E. R. Treasure, M. A. Vali, G. S. Watson, J. B. R. Wells, A. O. Wilson, C. G. Wilson, A. I. Yashruti.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on October 5, with the President, Dr. Andrew Allison, in the chair, Tayi Anjaneyulu Naidu, M.B., B.S., was admitted a Fellow of Faculty *qua* physician.

At the annual meeting of the Faculty held on November 2 the following office-bearers were elected for the ensuing year: *President*, Dr. Andrew Allison; *Visitor*, Professor Stanley G. Graham; *Honorary Secretary*, Dr. A. H. Imrie; *Honorary Treasurer*, Mr. Matthew White; *Honorary Librarian*, Dr. Archibald L. Goodall; *Representative on the General Medical Council*, Dr. Andrew Allison.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following were admitted to the Licence and Membership of the College on November 6, 1953: C. P. Gore, R. L. McCorry, M. K. O'Driscoll.

G. Bheek was admitted, *in absentia*, to the Licence and Membership on October 2, 1953.

The following candidates were admitted to the Licence of Medicine and Midwifery of the College on July 3, 1953: A. Omololu, A. Onyejiaka.

SOCIETY OF APOTHECARIES OF LONDON

The following candidates, having completed the final examination, are granted the diploma of the Society (L.M.S.S.A.), enabling them (upon complying with the requirements of the Medical Acts) to practise medicine, surgery, and midwifery: H. N. Orgel, N. G. Brockbank, B. Hatchick, D. J. Cripps, E. Jaques, G. L. Feldman, J. W. Jordan, B. N. Baijal, R. A. Rossdale, P. Sykes, E. R. Griffiths, G. C. Smith, A. Glover, J. B. Kriechbaum, J. K. Blackwell.

Dr. H. Seaward Morley, Master, presided at a recent meeting of the Court of Assistants of the Society, at which Dr. J. P. Hedley was reappointed Representative on the General Medical Council.

W. A. W. Dutton has passed the examination for the diploma of Mastery of Midwifery.

The following candidates, having completed the final examination, have been granted the diploma of L.M.S.S.A.: C. S. Chou, R. L. Cort, W. C. Newport, M. E. B. Carson, I. K. Nasr, W. P. N. Moore, A. C. Parry, P. M. C. Camm, E. C. Duerksen, J. D. Van Aswegan, D. S. Pickup.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College held on October 16, with the President, Mr. Arthur A. Gemmell, in the chair, the following were admitted to the Membership: L. J. Abramowitz, S. Alankaram, W. J. R. Anderson, G. S. Andrew, A. K. Bose, J. C. Brace, T. J. Buckley, S. Burke, R. K. Burt, J. G. Cameron, R. S. Casement, Po Wong Christina Chow, Maureen D. Connolly, R. L. Edwards, M. B. Flanagan, F. M. C. Forster, Kathleen M. Frith, M. C. G. Grant, P. B. Guastalla, R. H. J. Hamlin, J. W. S. Harris, J. M. Holmes, C. A. Jones, R. Ll. Jones, I. R. Macdonald, Betty Mallace, G. A. Manly, D. N. Menzies, M. C. Michelow, J. J. Nattrass, H. H. Neifeld, F. N. Neser, J. P. O'Dwyer, D. R. Patnaik, Clara Phillips, B. G. Pickles, W. Rotheram, J. S. Scott, J. M. Stewart, R. A. Struthers, Valerie M. Thompson, C. J. Thornberry, H. Ulman, C. G. Wilson.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been granted the diploma of L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.S.Glasg.: J. A. Childs, J. C. Douglas, E. Haniford, S. Khosla, T. J. McA. Kirby, G. D. B. Lindsay, P. Murray, Marie J. Ribchester, M. H. Rizvi, W. J. Ross, R. M. Wight.

CONJOINT BOARD IN IRELAND

The following candidates were successful at the D.P.M. examination held in September: L. I. Shenken, R. E. Jenkins, T. H. Bewley, H. M. Flanagan, D. D. Ellis, J. A. Kelleher.

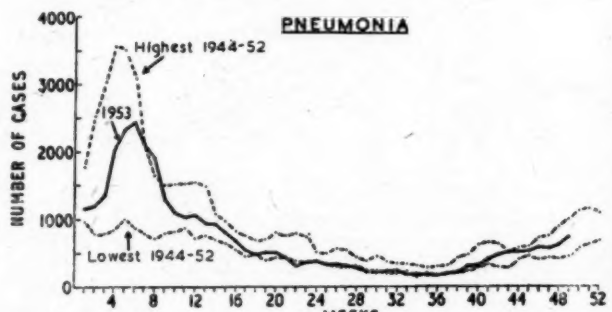
Vital Statistics

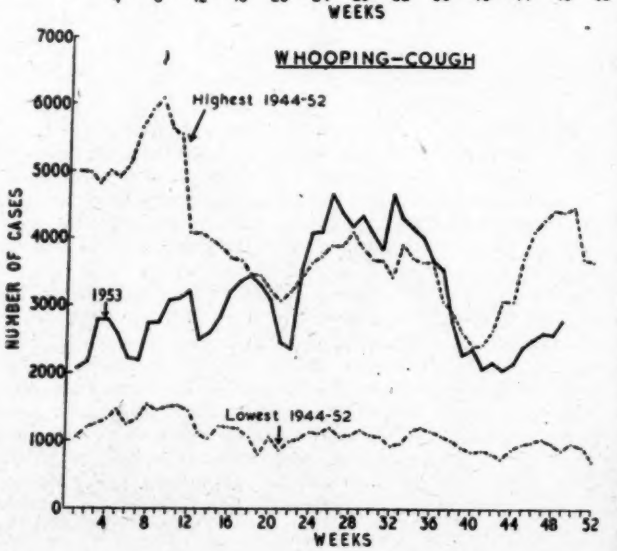
Week Ending December 19

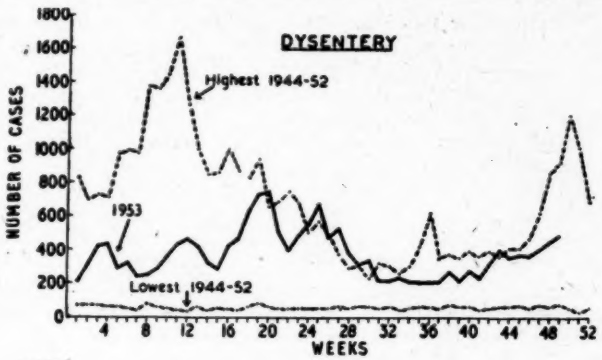
The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,284, whooping-cough 2,304, diphtheria 16, measles 778, dysentery 503, acute poliomyelitis 51, paratyphoid fever 4, and typhoid fever 1.

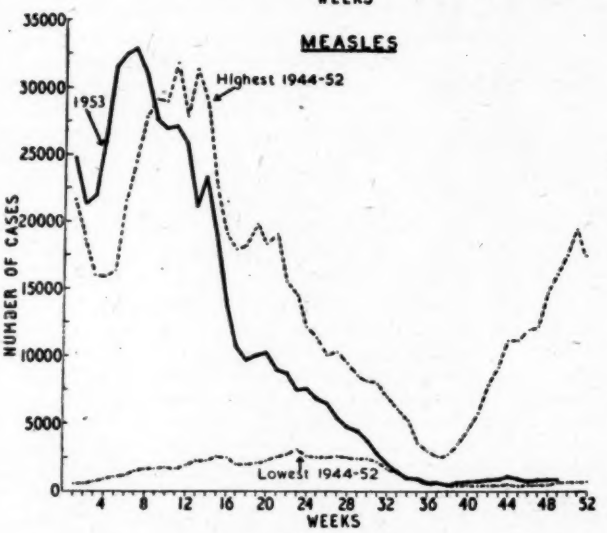
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest variations in the trends of infectious diseases in England and Wales during the week ending December 12 were increases of 161 in the number of notifications of whooping-cough, from 2,595 to 2,756, and 126 for acute pneumonia, from 614 to 740, and a decrease of 103 for scarlet fever, from 1,549 to 1,446.

No large variations were reported in the local trends of scarlet fever. The only fluctuations of any size in the returns of whooping-cough were an increase of 66 in Lancashire, from 267 to 333, and a decrease of 36 in Warwickshire, from 179 to 143. The incidence of measles has been practically constant for the past three weeks, and the 883 cases notified during the week were 3 fewer than in the preceding week. The only changes of note in the local trends were an increase of 64 in Lancashire, from 128 to 192, and a decrease of 46 in Yorkshire West Riding, from 73 to 27. 21 cases of diphtheria were notified during the week, an increase of 8 on the total of the preceding week. The chief features of the returns were an increase in Middlesex from 0 to 3 and a decrease in Warwickshire from 5 to 1. 7 of the 13 cases were notified in Staffordshire (Coseley U.D. 4).

59 cases of acute poliomyelitis were notified. These were 3 fewer for both non-paralytic and paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 9, Gloucestershire 5 (Bristol C.B. 5), Lancashire 5, London, 4, Hertfordshire 4, Warwickshire 4 (Birmingham C.B. 3).

485 cases of dysentery, 40 more than in the preceding week, were notified. The largest centres of infection were London 89 (Islington 15, Southwark 15), Lancashire 73 (Manchester C.B. 29, Bolton C.B. 25), Yorkshire West Riding 61 (Leeds C.B. 24, Bradford C.B. 21), Essex 34 (Colchester M.B. 9), Leicestershire 29 (Leicester C.B. 27), Norfolk 25 (Norwich C.B. 24), Surrey 25 (Frimley and Camberley U.D. 19), and Lincolnshire 23 (Cleethorpes M.B. 10).

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 12** (No. 49) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng & Wales	Lond	Scot.	N. Ire.	Eire	Eng & Wales	Lond	Scot.	N. Ire.	Eire
Diphtheria	21	2	2	0		29	4	6	0	1
Dysentery	485	89	167	5	3	259	21	69	2	1
Encephalitis, acute	1	0	0	0		5	1	0	0	
Enteric fever:										
Typhoid	1	0	0	0	1	3	0	0	0	1
Paratyphoid	5	0	1	0		4	0	0	0	
Food-poisoning	139	20		0		55	5		0	
Infective enteritis or diarrhoea under 2 years				10	13				6	13
Measles*	883	17	47	12	93	16,207	719	239	24	73
Meningococcal infection	27	1	11	0	1	33	2	13	1	4
Ophthalmia neonatorum	35	3	3	0		36	6	7	0	
Pneumonia†	740	60	231	27	1	719	61	433	5	2
Poliomyelitis, acute:										
Paralytic	46	2	10	7	5	48	3	4	1	2
Non-paralytic	13	2				10	1			
Puerperal fever§	224	31	13	1		215	39	8	1	0
Scarlet fever	1,446	76	234	35	62	2,259	171	314	36	88
Tuberculosis:										
Respiratory			135	27				122	22	
Non-respiratory			19	3				23	1	
Whooping-cough	2,756	124	382	74	60	2,067	104	99	29	104

DEATHS in Great Towns	1953					1952				
	Eng & Wales	Lond.	Scot.	N. Ire.	Eire	Eng & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	1		0
Dysentery	0	0		0		0	0			
Encephalitis, acute		0			1		0			0
Enteric fever	0	0	0	0		0	0			
Infective enteritis or diarrhoea under 2 years	10	0	0	1	1	11	0	0		0
Influenza	27	5	2	0	0	28	2	4		2
Measles		0	0	0	0		0			1
Meningococcal infection		1	0				0			
Pneumonia	247	34	17	8	7	303	45			3
Poliomyelitis, acute	2	0			0	3	0			0
Scarlet fever		0	0	0	0		0			0
Tuberculosis:										
Respiratory	111	13	12	2	6	147	14	26		8
Non-respiratory		0	2	1	2		7	2		1
Whooping-cough	3	0	1	1	1	0	0			0
Deaths 0–1 year	242	35	17	9	15	247	28	30		9
Deaths (excluding stillbirths)	5,130	711	589	105	158	6,647	945	834		194
LIVE BIRTHS	6,826	1094	792	183	294	6,883	986	817		440
STILLBIRTHS	179	23	22			173	15	27		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Epileptics and Spastics.—The special welfare needs of those suffering from epilepsy and cerebral palsy are dealt with in two reports, issued under the same covers, which have been sent by the Ministry of Health to all hospital, local health, and welfare authorities in England and Wales. The reports are the work of two committees appointed by a committee of the Ministry's Advisory Council on the Welfare of Handicapped Persons. The one concerned with epileptics had Professor Fraser Brockington as its chairman, and included among its members Dr. Denis Williams and the late Dr. J. Tylor Fox; and the other, which studied the problems of spastics, had Mr. E. S. Evans, F.R.C.S., as chairman, and Dr. L. T. Hilliard, Professor J. M. Mackintosh, Dr. Jean Mackintosh, and Dr. Denis Williams among its members. Dr. J. D. Spillane, in addition to the two chairmen, was a member of the appointing committee. The report, entitled "The Special Welfare Needs of Epileptics and Spastics" (Circular 26/53), is obtainable from Her Majesty's Stationery Office, price 1s. 3d. net.

King Edward's Hospital Fund for London.—Speaking of the Fund's new staff college for matrons at the meeting of the general council on December 17, the Duke of Gloucester appealed to hospitals not to grudge sparing their most promising sisters for the 10-months course at the college. "I should like to say," he declared, "that the future of the new staff college must depend to a great extent on the quality of those who participate in the first few courses." The staff college (at 22, Holland Park, London) opened last September and the first course there is already in progress. The Duke said that no large innovations were proposed in the allocation of funds for 1954. The pattern would be similar to that in recent years. The practice of visiting hospitals had been resumed. It provided an invaluable background against which the Fund could measure the relative importance of different projects. Sir Edward Peacock, treasurer of the Fund, said that the Fund had undertaken to bear the whole cost (estimated at £35,000) of providing the Thyroid and Endocrine Unit at New End Hospital with an extension for work on radioactive isotopes. The unit was, he said, the largest centre in Britain for the treatment of thyroid disease. Sir Archibald Gray, chairman of the distribution committee, said that the grants made by his committee during 1953 had totalled £120,000. Sir Ernest Pooley, chairman of the management committee, said that this year £50,000 was being made available for grants to mental hospitals as against £46,000 in 1953. The needs of the mental hospitals were particularly pressing. Lord Horder concluded the proceedings by proposing a vote of thanks to the Duke of Gloucester for presiding.

Life Insurance Medical Research Fund.—Exactly a year ago (January 3, 1953, p. 52) we reported the establishment of the Life Insurance Medical Research Fund of Australia and New Zealand by the Life Offices' Association for Australasia. Now details are available of the conditions under which grants-in-aid to institutions and research fellowships will be awarded. For the present it is intended to limit the resources of the Fund to the support of research on cardiovascular function and disease. Grants-in-aid will usually range from £1,000 to £3,000 a year, although in special circumstances larger grants may be made. Research fellowships tenable in Australia or New Zealand will be at the rate of £1,250 to £1,500 a year, while travelling fellowships, which will allow two years abroad followed by a third year in an approved institution in Australia or New Zealand, will range from £1,500 to £2,000 a year with certain travelling expenses. Further details may be obtained from Dr. John H. Halliday, Life Insurance Medical Research Fund of Australia and New Zealand, 87, Pitt Street, Sydney, Australia. The last date for applications for grants-in-aid and fellowships is June 1, 1954.

Animals for Research.—The Laboratory Animals Bureau has performed a useful service to research workers by publishing a stencilled catalogue of uniform strains of laboratory animals maintained in Britain. The catalogue gives details of the origin, pedigree, and management of 30 strains of mouse, 24 strains of rat, 8 strains of guinea-pig, 7 strains of rabbit, and 6 miscellaneous species. Although the catalogue is at present limited to vertebrates, the possibility of including invertebrates in the future is not ruled out. The main criterion for inclusion is that the strain should exhibit "a useful degree of uniformity." The catalogue, for which free additions and amendments will be issued from time to time, costs 2s. 6d. (post free), and is obtainable from the Laboratory Animals Bureau, M.R.C. Laboratories, Holly Hill, Hampstead, London, N.W.1.

Wernher Research Unit on Deafness.—Up to the present this Medical Research Council Unit has been located at the Royal National Throat, Nose, and Ear Hospital, Golden Square, London, under the direction of Dr. T. S. Littler. The unit is supported by funds from the Alexander Pigott Wernher Memorial Trust, and is concerned with the investigation of the medical and physical aspects of deafness. The unit has now moved to King's College Hospital Medical School, London, where Mr. Terence Cawthorne will act as honorary clinical director. Dr. Littler will continue as director of the unit.

National Fund for Poliomyelitis Research.—This lay money-raising body, founded a year ago, has issued its first report. The Fund has as its object the "promotion of research into the cause, prevention, cure, and treatment of poliomyelitis." In order to avoid the risk of supporting purposeless or impracticable projects, the Fund has adopted the admirable procedure of consulting with the Medical Research Council before allocating any grants. Last year the Fund provided £2,500 for the purchase of equipment required at the Central Public Health Laboratory, Colindale, for work in connexion with the preparation of a vaccine against poliomyelitis; £500 per annum for two years for the expenses of a committee (appointed by the M.R.C.) to co-ordinate investigation into the place of rest and exercise during convalescence after the disease; and £3,100 for equipment for studies at the London School of Hygiene and Tropical Medicine on the relationship of viruses to their host cells. The Fund is aiming to collect £250,000.

Cigarettes and Lung Cancer.—According to the *New York Times*, the Governor of New York, Mr. Dewey, is to ask the State legislature to include provision in their 1954–5 budget for research on the relationship of cigarette-smoking to cancer of the lung. This will form part of a two million dollar programme for all types of cancer research. In New York the death rate from lung cancer in males is reported to have risen nearly fivefold in the last 30 years.

Fever Hospital in Dublin.—Last month the Minister for Health, Dr. Ryan, opened a new fever hospital for Dublin at Clondalkin, County Dublin. It has cost £1,000,000 to build and replaces the former Cork Street Fever Hospital. The new hospital has eight ward blocks with 26 beds in each and three isolation blocks with 28 beds each. In addition there are a church, shop, laundry, garages, and administrative offices.

Chair of Physiology of Reproduction.—The vice-chancellor of Cambridge University has announced the bequest by the late Dr. F. H. A. Marshall of his residuary estate (estimated at £28,000) to the University. The bequest is subject to a life interest, and the funds are being held in trust for the foundation of a Mary Marshall professorship in the physiology of reproduction. Dr. Marshall, who was a Fellow of Christ's, was noted for his work in this field.

Industrial Nurses.—In our advertisement columns this week (p. 42) the Royal College of Nursing announces details of three special examinations for the Industrial Nursing Certificate. These will be open to general trained State-registered nurses with a minimum of five years' full-time industrial nursing experience.

COMING EVENTS

Sao Paulo Quatercentenary.—To celebrate the fourth centenary of the city of São Paulo the São Paulo Medical Association has organized 10 medical congresses to take place in the city during July, 1954. The congresses are: sixth International Congress on Cancer, nineteenth International Congress on Oto-Neuro-Ophthalmology, third Interim Congress of the Pan-American Association of Ophthalmology, fifth Pan-American Congress on Gastroenterology, first Latin-American Congress on Mental Hygiene, fourth Pan-American Congress on Puericulture and Paediatrics, second Latin-American Congress on Gynaecology and Obstetrics, twelfth Brazilian Congress on Cardiology, first Brazilian Congress on Physical Anthropology, and the third meeting of the Brazilian Society of Crenology and Climatology. Further details about any of these congresses may be obtained from the secretary of the São Paulo Medical Association, Caixa Postal 2103, São Paulo, Brazil.

French Medical Week.—"Les Journées Médicales de France," organized by the Société Médicale des Praticiens, will be held in Paris from April 21 to 25 under the chairmanship of Professor Camille Lian. The "Journées" are open to doctors and medical students of all countries. Further information may be obtained from the Secrétariat des Journées Médicales de France et de l'Union Française, 12, rue Pierre Geofroix, Colombes (Seine).

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, January 4

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. Michael Kremer: Research in Neurology.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Myopia, and the Care and Treatment of the Myopic Patient.
WEST LONDON HOSPITAL.—6 p.m., Professor T. Gualtierotti: Physiological Observations on Stimulating the Brain through External Electrodes in the Baboon and Man (illustrated by lantern slides).

Tuesday, January 5

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. M. S. Thomson: Diseases Due to Animal Parasites.

Wednesday, January 6

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Moniliasis.
ROYAL EYE HOSPITAL.—5.30 p.m., Mr. L. H. Savin: Ophthalmic Operations and their Indications (2).
YORKSHIRE SOCIETY OF ANAESTHETISTS.—At General Infirmary at Leeds, 8 p.m., Symposium arranged by Dr. H. J. Brennan.

Thursday, January 7

FACULTY OF HOMOEOPATHY.—5 p.m., Mr. H. D. W. Powell: Some Surgical Aspects of Fluid Balance.
●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Dr. E. M. Creak: Differential Diagnosis of Backwardness.
INSTITUTE OF PSYCHIATRY.—5.30 p.m., Inaugural Lecture by Professor G. W. Harris, F.R.S.: Emotional States and the Pituitary Gland.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., symposium: Overcoming Disabilities. Openers, Dr. C. A. Clarke, Dr. R. R. Hughes, Dr. A. Thelwall Jones, Dr. G. Sanderson, and Mr. G. E. Thomas.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. E. W. Riches: Recent Trends in Urology.
ROYAL EYE HOSPITAL.—5.30 p.m., Miss M. Savory: Differential Diagnosis of Proptosis.
ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.—4.30 p.m., demonstration of clinical cases; 5.15 p.m., discussion of clinical cases.

Friday, January 8

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. M. B. MacKenna: Psoriasis.
ROYAL EYE HOSPITAL.—5 p.m., Miss M. Savory: Differential Diagnosis of the Retinopathies.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Hill.—On December 16, 1953, at Robinson Hospital, Ballymoney, to Nancy (formerly Hinchcliff), M.B., wife of Dr. W. J. C. Hill, a daughter.
Persey.—On December 11, 1953, at Mortimer House, Bristol, to Dorothy Joyce (formerly Blake), M.B., Ch.B., wife of Alexander Persey, M.B., M.R.C.O.G., a daughter—Nicola Susan.

DEATHS

Benton.—On December 15, 1953, at 228, Old Shoreham Road, Hove, Sussex, Austin Lewis Benton, M.B., B.S.
Crofton.—On December 11, 1953, at Hertford, Herts, John Hutchinson Crofton, M.B., B.Ch.
Dobbin.—On December 15, 1953, Dorothy Isobel Dobbin, M.D., D.P.H.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Is Penicillin Alone Enough for Contaminated Wounds?

Q.—*If penicillin is given within a few hours of a contaminated laceration, can antitetanus and anti-gas-gangrene sera be omitted?*

A.—No. Tetanus antitoxin should be given for a dirty wound regardless of any chemotherapy. Whether penicillin treatment removes the need for gas-gangrene antitoxin is more debatable and dependent on the circumstances of the individual case. Army experience during the Battle of Europe is usually held to have proved that penicillin given systemically in adequate doses for several days will prevent gas gangrene. If penicillin is to be relied on in the treatment of a wound involving any serious risk of this infection the administration should be continued for four or five days. Adequate initial surgical treatment is assumed.

Treatment of Spidery Superficial Venules

Q.—*Several women patients have lately sought my advice on the finely meshed superficial varicose venules which appear after childbearing. The purplish areas occur above and below the knee. There is usually a small dilated vein just above the affected area, lying very superficially in the skin. Would injection of the dilated vein be effective in improving the appearance, and would it be safe?*

A.—The small spidery superficial venules occurring in women are by no means confined to those who have borne children. The lower part of the thighs and the upper part of the calves are the areas most often affected, and in general the venules are associated with a moderate amount of subcutaneous fat.

The affected areas are purplish in colour and of varying size, and when examined carefully or through a lens the appearance is seen to be due to a leash of very fine vessels. At the upper limit of the leash it is usually possible to find a small, thin-walled, cutaneous or subcutaneous vessel connected with the leash, while in some instances a vessel may be made out at the lower pole. The skin in the vicinity of the leash is thin and may show a little pigmentation. These areas of superficial vessels may exist alone, or they may be associated with actual varicosities or incompetence of larger veins. The affected areas usually tend slowly to increase in size, and give rise to progressive discoloration. The skin may be slightly sensitive, and some patients are prone to subcutaneous ruptures of the venules, giving rise to large bruised areas.

It is important from the point of view of treatment to determine whether or not the condition exists alone or is associated with changes in the larger veins, as in the latter event treatment of the superficial venules must be considered in relation to that of the larger veins. Treatment is rarely necessary when the superficial venules exist alone, but it may at times be advisable on account of the progress of the condition, local discomfort, relationship to varicose eczema, or for cosmetic reasons.

Injection treatment of any feeding veins is the only method of any value, and the effect of this is mainly to delay the progress of the discoloration. Some diminution in discoloration may follow successful treatment, but usually some of the skin changes are irreversible. Patients should never be told that treatment will get rid of all the discoloration.

Injection treatment of venules of this type is best left to the expert. The intravenous technique must be certain, a very fine needle is essential, and minutes doses of injection

fluid must be used. The veins that are being injected are very thin-walled and are often covered by a very thin layer of epithelium. For these reasons, even with the most careful intravenous technique, it is possible that the overlying epithelium may not be strong enough to withstand even a mild inflammatory reaction following the injection of a minute dose of sclerosant.

Is Bell's Palsy Infectious?

Q.—*I have encountered three cases of facial palsy in rapid succession in my practice. Is this just a coincidence, or is the condition infectious?*

A.—The aetiology of the common facial palsy (Bell's palsy) is not known for certain, but many people consider it is probably infective in nature. Small groups of cases occurring together in a locality are not rare.

Home Electrolysis

Q.—*Home electrolysis outfits for the removal of superfluous hair are now on the market. Are these suitable to recommend to patients for use in their own homes?*

A.—The chief danger with electrolysis is over-treatment. In most cases the current needs to be passed for only a few seconds, and if the needle is held in place with the current passing for too long there results an excessive area of necrosis leading to a slough, perhaps a millimeter or so in diameter. This can only result in a scar. It does not seem very likely that a patient treating herself will cause this kind of damage provided that she is sensible and properly advised by her doctor. Infection is never likely to be a serious problem provided elementary precautions of cleanliness are taken; in any case this risk seems no more likely in the home than in a beauty parlour.

It is not, of course, every person who will be able to acquire the manual dexterity for carrying out this rather delicate operation; the seven-day free trial period should be sufficient to enable a patient to decide about this. Self-treatment of hairs on the front and central part of the face is easy for the patient herself; at the side of the cheeks not so easy; and under the chin, where superfluous hair is often present, a very difficult task.

Prickly Heat

Q.—*What is the aetiology of prickly heat? What are the main diagnostic features distinguishing it from other skin rashes? What is the most successful treatment?*

A.—Prickly heat is generally held to be caused by blockage of sweat ducts by keratinous plugs. Sweat is thus held back in the glands and is responsible for the papular rash. Prolonged sweating with maceration of the cells in the horny layer of the skin is the commonest precursor, but injury caused by ultra-violet light, application of chemicals, or adhesive plaster may act in a similar way. The relationship of sodium to the aetiology of the condition remains rather in doubt.

The diagnostic features are the appearance of the rash after a period of at least several days' exposure to high environmental temperature, especially if the atmosphere be humid. The body flexures, chest, back, shoulders, and abdomen are the commonest sites affected, and the rash is almost invariably symmetrical. Seborrhoeic dermatitis may sometimes be simulated, but the history and aggravation of symptoms while sweating are distinctive features of prickly heat, while there are no macular or plaque-like lesions such as are common in seborrhoeic dermatitis. In miliarial rashes caused by various local applications the distinguishing characteristics are the more limited distribution and history of exposure to the agent concerned.

Innumerable powders and lotions are recommended for the treatment of the condition, their very multiplicity being testimony of their ineffectiveness, while some of them may lead to a complicating dermatitis medicamentosa. Measures taken to keep cool and to avoid sweating alone are likely to be effective—that is, the use of fans, light loosely fitting clothing, and the avoidance of excessive exercise, particularly during the warmer parts of the day.

Incest: Marriage to a Sister-in-Law

Q.—(*a*) *With what relatives is it incestuous to cohabit?* (*b*) *Does the law allow marriage between a divorced man and his former sister-in-law?*

A.—(*a*) Under the Punishment of Incest Act, 1908, Section 1 (i), a male person who has carnal knowledge of a female who is to his knowledge his granddaughter, daughter, sister, or mother, is guilty of a misdemeanour. Under Section 4 a female of or above the age of 16 who permits a person who is to her knowledge her grandfather, father, brother, or son to have carnal knowledge of her is guilty of a misdemeanour.

(*b*) The Deceased Wife's Sisters' Marriage Act, 1907, permits the marriage, in so far as it is a civil contract, of a man with his deceased wife's sister. It is unlawful for a man to marry the sister or half-sister of his divorced wife or of his wife by whom he has been divorced during the lifetime of the wife, or the divorced wife of his brother or half-brother, or the wife of his brother or half-brother who has divorced his brother during the lifetime of the brother or half-brother.

Parotid Enlargement in Primitive Peoples

Q.—*Is there any explanation of the bilateral chronic enlargement of the parotid glands found in primitive peoples in various parts of the world? Here in Borneo it occurs not uncommonly in the Murut tribes: it arises in childhood and is definitely not due merely to an increase in adipose tissue. Mumps is not uncommon among these tribes: could that be the cause?*

A.—Enlargement of the parotid glands has latterly been recognized as one of the results of protein deficiency, and it is unlikely that mumps is responsible in the cases in question. Other organs developmentally similar to the parotids, such as the salivary and lacrimal glands and the pancreas, may also be damaged. In malignant malnutrition, kwashiorkor, and allied syndromes parotosis is not uncommon.

Glycerin in Obesity

Q.—*Can glycerin be used as a sweetening agent in the treatment of obesity?*

A.—Glycerin is largely converted to glucose in the body. There would therefore seem to be no theoretical basis for its use in obesity.

"Any Questions?" Book.—The second book of selected "Any Questions?" is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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